COMPARISON OF TWO DIFFERENT DOSES OF CLONIDINE WITH ULTRASOUND GUIDED CAUDAL FOR POST OPERATIVE PAIN RELIEF IN CHILDREN.

DISSERTATION SUBMITTED FOR THE DEGREE OF

DOCTOR OF MEDICINE

BRANCH – X (ANAESTHESIOLOGY)

APRIL 2015

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI,

TAMILNADU

CERTIFICATE FROM GUIDE

This is to certify that this dissertation entitled **"COMPARISON OF TWO DIFFERENT DOSES OF CLONIDINE WITH ULTRASOUND GUIDED CAUDAL FOR POST OPERATIVE PAIN RELIEF IN CHILDREN."** is a bonafide record work done by **Dr.D. AMBIKAI** under my direct supervision and guidance, submitted to the Tamil Nadu Dr.M.G.R.Medical University in partial fulfillment of University regulations for MD, Branch X– Anaesthesiology.

PROF.Dr.T.THIRUNAVUKKARASU M.D.,D.A.,
Institute Of Anaesthesiology,
Govt.RajajiHospital&MaduraiMedicalCollege
Madurai.

Dr. M.SHANMUGA SUNDARAM M.D
Assistant professor
Institute Of Anaesthesiology,
Govt.RajajiHospital&MaduraiMedicalCollege
Madurai.

CERTIFICATE FROM DIRECTOR & H.O.D

This is to certify that this dissertation entitled **"COMPARISON OF TWO DIFFERENT DOSES OF CLONIDINE WITH ULTRASOUND GUIDED CAUDAL FOR POST OPERATIVE PAIN RELIEF IN CHILDREN."** is a bonafide record work done by **Dr.D. AMBIKAI** under my direct supervision and guidance, submitted to the Tamil Nadu Dr.M.G.R.Medical University in partial fulfillment of University regulations for MD, Branch X– Anaesthesiology.

PROF. Dr.S.C.GANESH PRABU, M.D, D.A,

Director,

Institute Of Anaesthesiology,

Govt.RajajiHospital&MaduraiMedicalCollege

Madurai.

CERTIFICATE FROM DEAN

This is to certify that this dissertation entitled **"COMPARISON OF TWO DIFFERENT DOSES OF CLONIDINE WITH ULTRASOUND GUIDED CAUDAL FOR POST OPERATIVE PAIN RELIEF IN CHILDREN."** is a bonafide record work done by **Dr.D. AMBIKAI** under my direct supervision and guidance, submitted to the Tamil Nadu Dr.M.G.R.Medical University in partial fulfillment of University regulations for MD, Branch X– Anaesthesiology.

Dr. B.SANTHAKUMAR M.D

DEAN

GOVT. RAJAJI HOSPITAL &MADURAI MEDICAL COLLEGE

MADURAI

DECLARATION

I, **Dr.D.AMBIKAI**solemnly declare that, this dissertation titled"**COMPARISON OF TWO DIFFERENT DOSES OF CLONIDINE WITH ULTRASOUND GUIDED CAUDAL FOR POST OPERATIVE PAIN RELIEF IN CHILDREN.**"has been done by me. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree or diploma to any other University or board either in India or abroad. This is submitted to The Tamilnadu Dr. M. G. R. Medical University, Chennai in partial fulfillment of the rules and regulation for the award of Doctor of Medicine degree Branch –X (Anaesthesiology) to be held in April 2015.

Place: Madurai **Dr. D.AMBIKAI**

Date:

ACKNOWLEDGEMENT

I am greatly indebted to **Dr.S.C.GANESH PRABU M.D., D.A.,**Director and Head of the Institute of Anaesthesiology, Madurai Medical College, Madurai for his guidance and encouragement in preparing this dissertation.

My heartful thanks to **Dr. T.THIRUNAVUKKARASU M.D.,D.A.,** Professor of Anaesthesiology, Madurai Medical College, Madurai for his guidance in doing this work.

I am thankful to my Professors **Dr.A. PARARMASIVAN, M.D., D.A., Dr.R.SHANMUGHAM.,M.D.,D.C.H., and DR.EVELYN ASIRVATHAM M.D., D.G.O., D.C.H**for their constant support and guidance in performing this study.

I also thank Assistant Professor **Dr. M.SHANMUGA SUNDARAM M.D.,** for his constant support in conducting this study.

My profound thanks to **Dr. B. SANTHAKUMAR M.D., Dean**, Madurai Medical College and Government Rajaji Hospital, Madurai for permitting me to utilize the clinical materials of this hospital for the completion of my dissertation.

I gratefully acknowledge the **patients** who gave their consent and cooperation for this study.

ABSTRACT

Caudal epidural analgesia with bupivacaine is very popular in paediatricanaesthesia for providing intra- and postoperative analgesia. Several adjuvants have been used for prolonging the action of bupivacaine.

We evaluated the efficacy of twodifferent doses of clonidine added to caudal bupivacaine in children undergoing infra-umbilical surgery for prolonging the duration of post operativeanalgesia.

50 children of age 2-6 years, undergoing infra-umbilical surgery were prospectively randomized into two groups ,

GROUP 1- bupivacaine 0.25% (1ml/kg) with clonidine 1 mics/kg .

GROUP 2 -bupivacaine 0.25% (1ml/kg) with clonidine 2 mics/kg.

Post-operative painwas assessed for 10 hours using the FLACC scale. The mean duration ofpost operativeanalgesia was significantly longer in Group -2(9.02±0.55 hrs) than in Group 1 (7±0.71 hrs); $P< 0.0001$ and is found to be statistically significant.

The pain score assessed using FLACC scale was compared between the two groups, and children in Group 2 had lower pain scores, which was statistically

significant at 10 hrs . The requirement of rescue medicine was lesser in Group 2. Clonidine in a dose of 2 mics/kg added to 0.25% bupivacaine for caudal analgesia, during infra umbilical surgeries, prolongs the duration of bupivacaine, than clonidine in a dose of 1mics/kg without any side effects.

Keywords: Bupivacaine, caudal analgesia, clonidine, post-operative analgesia, infra-umbilical surgery.

INTRODUCTION

An unpleasant sensory and emotional experience is defined as pain which is associated with actual or potential tissue damage .It is distinct from other modalities such as touch ,warmth ,and cold .It is a subjective sensation which can only be experienced and not expressed, especially in children. Humanitarian is the foremost treatment of any pain. It is important in children who depend on their parents for their well being. There is drastic change and improvement over the concept of postoperative pain relief especially in the paediatric age group.

All the methods of pain relieving techniques has some disadvantages which limits their use in children such as need of cautious use of opioids because of its respiratory depression effects , some analgesics cannot be given after general anaesthesia because of their adverse effects like vomiting and aspiration and due to fear of needles in case of parenterally administered analgesics.

Hence regional anaesthetic techniques was selected which decrease significantly not only post operative pain and but also systemic analgesic requirements. The simplest, safest technique among the regional techniques in paediatricsurgery was caudal ,it was selected for this study as it has a high success rate.

Caudal was performed under ultrasonogram guidance ,to avoid multiple needle pricks, for reducing intravascular or intrathecal complications and for improving the success rate of assessing epidural space in the first attempt. In children , epidural space allows rapid spread of drugs longitudinally ,and thereby postoperative pain is treated effectively.

In children one of the most acceptable and popular method of providing intra- and post-operative analgesia for infra umbilical surgeries is caudal block. The most commonly used local anaesthetic for caudal analgesia is bupivacaine . Shorter duration of action of about four to six hours during 'single shot technique' is the main disadvantage of Bupivacaine.

For prolonging the duration of post operative analgesia with bupivacaine several adjuvants like opioids, ketamine, midazolam, clonidine and neostigmine are used.

The most commonly used adjuvant with bupivacaine is clonidine for caudal analgesia. It is an alpha 2 agonist and it has been used for both central neuraxial blocks and peripheral nerve blocks with bupivacaine for prolonging its action.

This study was performed under ultrasound guidance in elective subumbilical surgeries to assess the efficacy of different doses of clonidine with bupivacaine for postoperative analgesia in children.

Clonidine is an mixed α1 and α_2 agonist but has an greater affinity for α_2 adrenergic receptors .The hypnotic and analgesic effects are mediated by α2a receptors.Clonidine improves the quality of anaesthesia, provides a more stable cardiovascular course during anaesthesia , mainly due to its sympatholytic effect and it reduces dosage of anaesthetic drugs.

Analgesic action is due to its stimulatory effect on inhibitory alpha 2 receptors and reduce the central neural transmission. It inhibits the release of substance –p.

HISTORICAL BACKGROUND

Epidural injection through sacral hiatus was described by SICARD and CATHELIN in the year 1901. In the year 1933 – CAMBEL M.F was the first to demonstrate in children and infants the sacral epidural block. In the year 1957 – The drug Bupivacaine was synthesized. In the year 1960 – Drug Clonidine hydrochloride introduced. In the year 1963- Clinically ,Bupivacaine was used.

Central neuraxial blockade under ultrasound guidance was first reported byBogin and Stulin.They were the first to describe lumbar puncture under ultrasound guidance in the year 1971. In the year 1978, ULTRASOUND was used by porter and colleagues for imaging the lumbar spine and for measuring the diameter of the spinal canal.. The first group of anesthesiologists to use USG for locating the landmarks for epidural anesthesia was Cork and his colleagues.Later, to preview the spinal anatomy and for measuring the epidural space and distances from the skin to the lamina before epidural puncture ultrasound was used .

Grau and coworkers,recently performed a series of studies and significantly contributes to the current understanding of spinal sonography

A two-operator technique was described by these investigators which consistsofvisualization of neuraxial space under ultrasound using a paramedian sagittal axis and for midline insertion of the needle to accomplish a combined spinal-epidural block. There is a much greater clarity during imaging of the spine and neuraxial structures due to recent advancement in ultrasound technology.

AIM OF THE STUDY

1. To Compare the efficacy of two different doses of clonidine with caudal bupivacaine.

2. Pain was assessed by FLACC scale.

3. Time of rescue analgesia(duration of analgesia) and the number of doses of rescue analgesia.

4. To evaluate the complications.

ANATOMY RELATED TO CAUDAL BLOCK

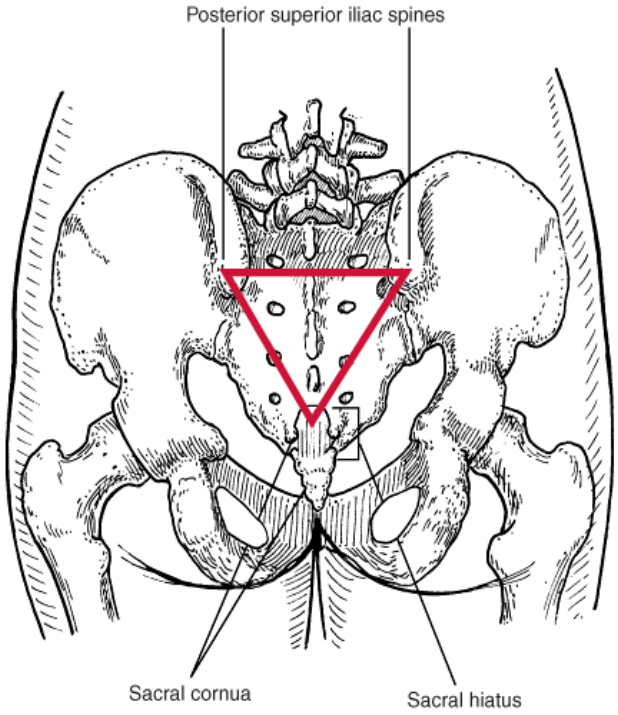
ANATOMY OF SACRUM

The fusion of five sacral vertebrae and articulating above with 5th lumbar vertebra and below with the coccyx,is the sacrum which is a wedge shape bone .It has concave anterior and convex posterior surfaces; the anterior surface bears four transverse lines (demarcating the boundaries between the fused bodies) which terminate on each side in four anterior sacral foramina. The anterior primary rami of the first four sacral spinal nerves, emerge from the anterior sacral foramina. The posterior surface is convex and in midline runs a bony ridge, the median sacral crest with 3 or 4 rudimentary spinous process.

The lamina of the 5th and sometimes the 4th sacral vertebra fuse fail to fuse in the midline.the deficiency thus formed is known as "**sacral hiatus** ". the lateral margins of this space each bear a prominence – "**sacral cornu**" – which represents the inferior articular process of the 5th sacral vertebra.

Sacral canal

It is a prismatic cavity running throughout the length of the boneand following its curves. Superiorly, it is triangular in its section and is continuous with the lumbar epidural space. Its lower extremity is the sacral hiatus, closed by posterior sacro -coccygeal membrane.



Fibrous bands may be present in the canal and divide the epidural space into loculi which prevent the spread of solution and these may account for occasional incomplete anaesthesia.

Sacral vertebrae were fused to form the anterior wall of sacral canal and fusion of laminae forms the posterior wall.

Sacral canal contents

1. Dural sac extends and ends at lower end of 2nd sacral vertebra on a line joining the posterior superior iliac spine.
2. Sacral and coccygeal nerve roots with their dorsal root ganglia.
3. The filumterminale which is the continuation of piameter
4. Epidural plexus of veins formed by the lower end of vertebral veins. These vessels are numerous in anterior aspect than posteriorly
5. Loose areolar and fatty tissue, which is more dense in males than in females

Sacral hiatus

This is a triangular opening present in the posterior wall resulting from failure of fusion of laminae of the 5th sacral vertebra. Its apex is at the level of the spine 4th sacral vertebra. In some cases the apex is at the level of 3rd sacral spine, due to the absence ofthe 3rd and 4th laminae and occasionally the whole of the bony posterior wall is deficient. When the laminae of the 5th sacral vertebra are present, the hiatus may be very small with a diameter of as narrow as 2mm.

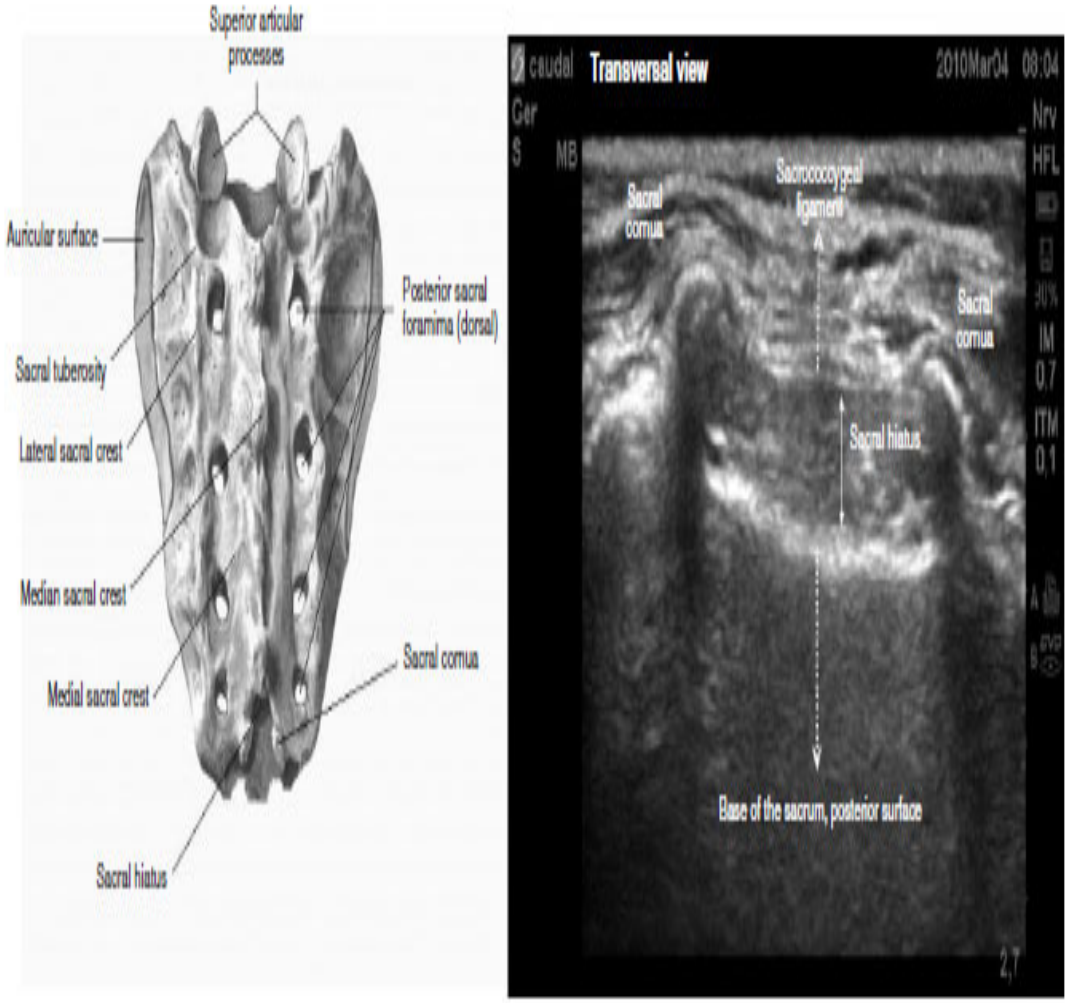
The hiatus is covered by the sacro-coccygeal membrane and pierced by the coccygeal nerves and the 5th sacral nerve. This membrane may be ossified in elderly subjects making the introduction of caudal needle difficult.

Ultrasonogram-guided caudal epidural anesthesia

Ultrasonogramof the sacrum should be done to identify the relevant sonoanatomy before caudal epidural injection. A high-frequency linear transducer should be used for superficial structures like sacrum.

In the level of sacral hiatus, with transversal sonogram two inverted U-shaped hyperechoiec structure on either side of midline is seen which denotes the two sacral corneal prominences. The hyper echoic band, denotes the sacrococcygeal ligament, connecting both sacral cornua. Anterior to the sacrococcygeal ligament another linear structure which is hyper echoic

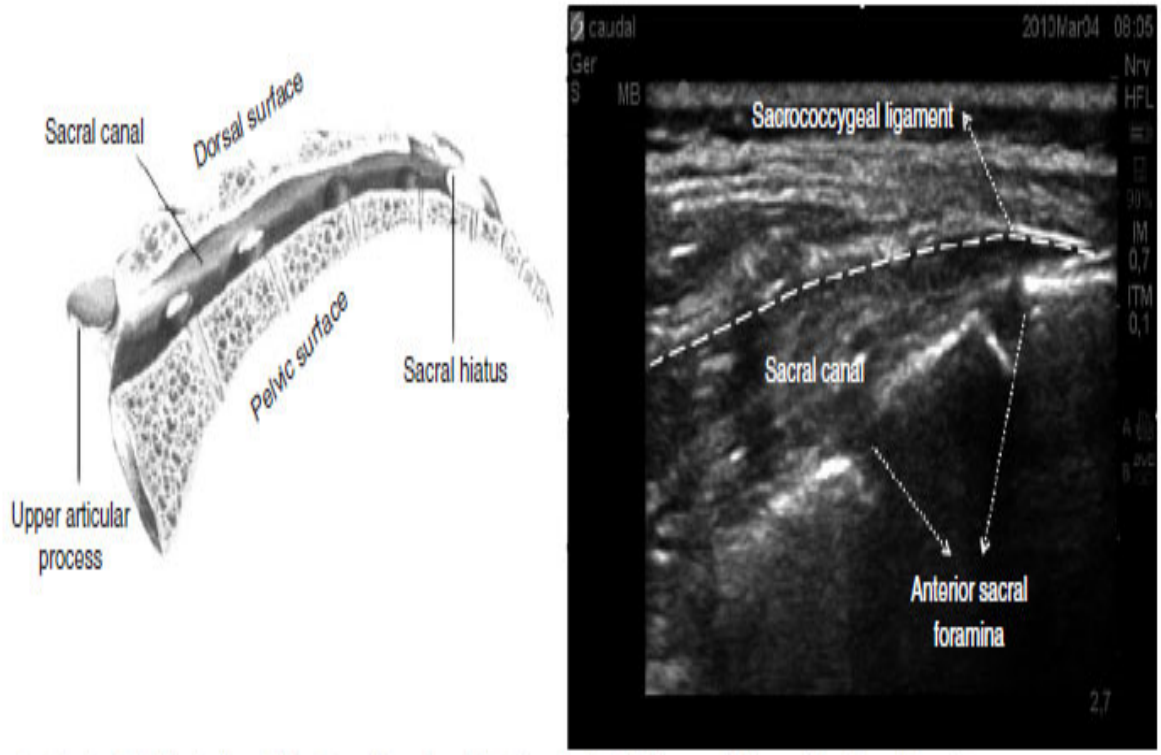
represents posterior surface of sacrum. In between the posterior sacral surface and sacrococcygeallgament is sacral hiatus which is hypo echoic.



In the level of sacral cornua, with help of sagittal sonogram the sacrococcygeal ligament, sacral hiatus, and sacral base can be visualized clearly. Sacrum is seen above sacral hiatus as hyper echoic band which is smooth with

wide anterior acoustic shadow. If the transducer is moved cephalad maintaining the same direction the space in between L5 and sacrum (paramedian sagittal scanning) denotes L5/S1 inter vertebral space .

.



the landmark of sacral hiatus with the help of sagittal transverse scanning using 6-13 mega hertz transducer which is high frequency is used for caudal epidural..

Both in plane and out of plane technique can be used for needle insertion. For in plane insertion, sagittal scanning is done and the needle is passed using real time visualization into the sacral canal passing through sacrococcygeal ligament.

However, a big acoustic shadow is present due to the sacrum, which hinders the ultrasound beam, which makes it hard to visualize the needle tip and drug dispersion in the canal.When local anaesthetic is injected into the sacral canal, it ascends upwards in the sacral epidural space for a distance proportional to the volume of the solution, force of injection, amount of leakage through the eight sacral foraminae and the connective tissue in the space.

PHYSIOLOGICAL CONSIDERATION

CLASSIFICATION OF PAIN

Pain can be classified ,

1. Pathophysiologically into nociceptive or neuropathic pain.
2. Etiologically into post operative or cancer pain.
3. Involvement of affected areas (headache or back pain)
4. Clinically into acute or chronic pain.

The term NOCICEPTION is from latin which means harm or injury.

Nociceptive pain is due to the activation of peripheral nociceptive receptors by the noxious stimuli. .Neuropathic pain is due to the abnormalities of the peripheral or central neural structures which is acquired or as a result of injury.

ACUTE PAIN

It is defined as the pain produced by the noxious stimuli as a result of injury or disease or due to the abnormal function of muscle or viscera. It is mainly nociceptive. It serves to detect and localize the pain.Transduction, transmission,modulation and perception are the four physiological process involved . Postoperative pain, post traumatic and pain due to medical illness (myocardial infarction, pancreatitis ,renal calculi) are some of the examples.

Acute pain is mostly self limiting or cured in treatment within days or weeks.

They are of two types .SOMATIC PAIN and VISCERAL PAIN.

SOMATIC PAIN

It is further divided into ,.Superficial pain.and.Deep pain.

SUPERFICIAL PAIN

It is caused by nociceptive stimuli from skin , subcutaneous tissues and mucous membranes.Characteristically , it is localized and often explained as throbbing, sharp and pricking or burning pain.

DEEP PAIN

It is caused by nociceptive stimuli arising from muscles,tendons and bones or joints. It is usually dull in quality and is poorly well localized.The degree of localization is affected by intensity and duration of stimulus. Pain due to injury to elbow joint is well localized than pain due to severe or sustained injury to the elbow.

VISCERAL PAIN

It is due to pathology of internal organs and their coverings (parietal pleura ,peritoneum and pericardium). It is further classified into ,.true localized visceral pain, localized parietal pain ,.referred visceral pain and referred parietal pain.

VISCERAL PAIN	PARIETAL PAIN
1.It is diffuse, dull and mostlymidline. 2.commonly associated with sympathetic or parasympathetic abnormality causingvomiting ,changes in blood pressure, heart rate and sweating.	1. It is usually sharp,stabbing and is localize or referred. 2. due to embryological development and migration of tissues ,pain is referred to areas distant from the diseased area.

CHRONIC PAIN

Pain persists after an average healing time or beyond the uaual time of any acute illness. It is usually last for 1- 6 months . Patients have sleep and and mood disturbances ,and have an attenuated neuroendocrine stress response. Osteoarthritis ,rheumatoid arthritis ,diabetic neuropathy, postherpetic pain are some of the examples.

DEAFFERENTATION PAIN

Pain that occurs without any sensory input into central nervous system is called as deafferentation pain

PAIN PATHWAYS

A noxious signal from periphery gets transferred to spinal cord through various peripheral nerves culminating finally in cerebral cortex.from there the descending impulse is sent to various peripheral nervous systems after

modulation at various places like periaqueductal grey matter ,pituitary gland, substansia gelatinosa and so on.

DIFFERENT TYPES OF PAIN RECEPTORS

The pain receptors are distributed throughout the body .Mainly two kind of receptors have been studied extensively. They are free nerve endings and opiate receptors.

1.FREE NERVE ENDINGS

The pain stimuli is received by peripheral receptors of skin,namely free nerve endings. These free nerve endings are the nociceptors. These are afferent nerve endings with tiny receptive fields, these nociceptors have high response thresholds and discharge persistently to stimuli which is suprathreshold and do not undergo rapid adaptation.

Nociceptive pain occurs due to stimulation of pain receptors called A-delta and C-polymodal receptors present in connective tissues, viscera, muscle, bone and skin by secondary stimulation by thermal, mechanical and chemical substances through algogenic substances like histamine, bradykinin, substance-P

. However, before reaching the brain these painful stimuli undergo several processing in the periphery and at the spinal cord.

2.OPIATE RECEPTORS

It has been found that pain produced by different injuries under different conditions in different people can be variable.the circuit where opioids involved are studied extensively. Opiates bind to the neurons in the periaqueductal grey matter,substansiagelantinosa,the trigeminal nuclei,reticular formation and thalamus led to the hypothesis that endogenous substances with analgesic properties similar to the opiates exist.These substances were called endorphins.Endorphins are concerned in pain modulation through principal mechanisms.

1. Descending pathways via the periaqueductal grey area of midbrain and raphe magnus nucleus.
2. Substansiagelatinosa.
3. Anterior pituitary gland.

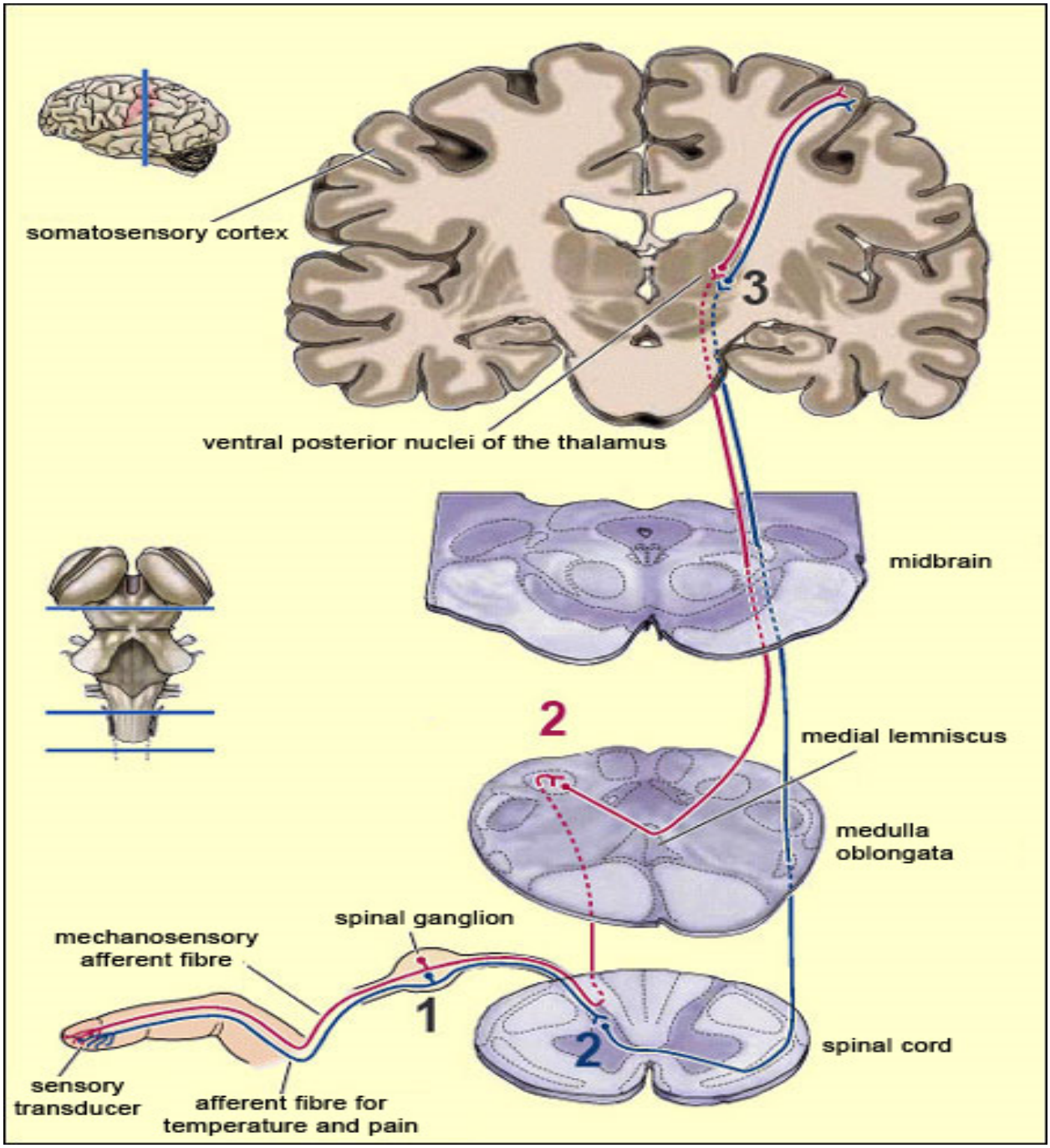
PAIN PATHWAYS

Two types of fibres involved in the conduction of pain from the periphery are A delta fibres and Cfibres. A delta fibres are myelinated and relatively rapidly conducting(12-30m/sec). They conduct the sharp pain produced by pin prick or electrical stimulation as well as thermal stimuli and responsible for withdrawal reflex.

A delta conducted pain is felt quickly and is well localised.‘C’ fibres are very fine non-myelinatedfibres which conduct at a very slow rate 2-3m/sec or less. Their threshold for stimulation is higher and is responsible for delayed and truly noxious burning or throbbing pain.

The activation of two different type of fibres(A delta &C) by noxious stimuli explains how a single short painful stimuli evokes double sensation in human beings: rapid pricking pain(0.1sec, latency, first pain) carried by A delta fibres is followed by, 1 sec later, approximately a burning pain (second pain) mediated through C fibres.

Primary afferent fibers are situated in the dorsal root ganglia, where it synapses with the second order neurons, their axons crosses midline ,and ascend along the spinothalamic tract to the thalamus, where it synapse with the third order neurons and through the internal capsule and corona radiate it sends projections to the postero lateral gyrus of the cerebral cortex.



SPINAL CORD GREY MATER DIVIDED INTO 10 LAMINA BY REXED

1. The first six lamina - principle site of pain modulation and they also receives all afferent neuronal activity.

Second order neurons are either ,Nociceptive specific –receives only noxious stimuli.Wide dynamic range neurons (WDR)neurons –receives both noxious and non-noxious stimuli from A alpha ,A delta and C fibres.Lamina 1 – nociceptive specific neurons are located .It respond to noxious stimuli from the cutaneous and deep somatic tissues.It also receives lesser amount of visceral afferents.Lamina 2 – also called substansiagelatinosa.-Involved in proceesing and modulating nociceptive input from cutaneous nociceptors.Lamina 3 and 4 – receives non-nociceptive input.

Lamina 5 – termination of most of the visceral afferents.it also receives somatic afferents. WDR neurons are more abundant here. Lamina 1 and 5 – represent the central convergence point between somatic and visceral input.Lamina 7 – contains cell bodies of preganglionic sympathetic neurons .Otherwise known as interomedialateral column. Lamina 8 and 9 – make up the anterior (motor) neuron.

SPINOTHALAMIC TRACT

It is the major pain pathway, situated anterolaterally in the white matter of the spinal cord. It is divided into lateral and medial spinothalamic tract.

LATERAL (NEO) SPINOTHALAMIC TRACT	MEDIAL(PALEO) SPINOTHALAMIC TRACT
1. Projects to the ventral posterolateral nucleus of thalamus. 2. Carries fibers that discriminate different aspects of pain such as its location, pain intensity and its duration.	1.projects to medial thalamus. 2.carries autonomic and unpleasant emotional perceptions of pain.

SPINOTHALAMIC FIBRES- also project into,

1. periaqueductalgray – forms an link between ascending and descending pathways.andintoreticular activating system and hypothalamus –which is responsible for arousal response to pain.

ALTERNATE PAIN PATHWAY :

1. SPINORETICULAR TRACT –mediate autonomic responses and awakening to pain.
2. SPINOMESENCEPHALIC TRACT –involved in initiating anti-nociceptive and descending pathways.
3. SPINOHYPOTHALAMIC AND SPINOTELENCEPHALIC : stimulate hypothalamus and mediate emotional behaviour.

4. SPINOCERVICAL : ascends to the lateral cervical nucleus. Relays fibres to contralateral thalamus. It is a major alternate pain pathway.

MECHANISM OF PAIN RECEPTORS ACTIVATION

Variety of mediators are involved in the process like arachidonic acid, prostaglandins,leukotriens.substance –P,Serotonin and others.

1.In the Periphery

Whenever there is a noxious stimuli in periphery producings intense pressure and causing cell damage , a cascade of events follows . The cell damage leads to a to low pH,potassium release and liberation of arachidonic acid from cell wall. These leads to synthesis of prostaglandins and bradykinins. Prostaglandins E and I sensitise pain receptors and PGEs are believed to be involved in the amplication of the pain in the inflammatory process. Through the neuro effector function these primary afferent nociceptors play vital role in tissue protection and thus, are not just messengers of tissue injury.

2. In The Spinal Cord and brain

After the primary activation ,the secondary activation sets in. stimulated terminals not only transmit impulses to spinal cord but also to other terminal nerve branches and induce the release of substances like peptides which includes substance- P. Substance –P produces vasodialation and causes accumulation of bradykinin producing neurogenic edema. Mast cells releasing histamine and platelets releasing seratonin is also mediated by substance- P.

The principal pain transmitter in the spinal cord is presumed to be substance-P.It is present in the dorsal root ganglion and dorsal horn .When inflammation or damaged tissue is present the threshold is lowered in primary afferent nociceptors, thus, repitative or prolonged or intensive stimuli is applied the frequency of firing is increased. Inflammatory mediators like leukotriens, prostaglandins contribute to this phenomenon called as sensitisation.In the sensitised tissues even normal innocuous stimuli produces pain. Tenderness, hyperalgia ane soreness are mainly due to sensitisation. Clinical pain involves both peripheral and central sensitisation thus cannot be precicely described as a patho physiological state.

Peripheral sensitisation is caused by the inflammatory response whereas central sensitisation due to plasticity responses in spinal cord dorsal horn neurons.

PAIN MODULATION

Pain signals arriving from periphery are send to areas of the brain where they stimulate the release of chemical substances,which reduce nociception or pain sensation.

The pain modulation takes place at periaqueductal grey matter,nucleus raphe magnus of brainstem ,spinal interneurons and others.Periaqueductal grey matter in mesencephalon –releases endorphins.Nucleus raphe magnus of brain stem-releases enkephalins .Spinal interneurons – release dynorphin.

ANTI-NOCICEPTIVE RECEPORS -1

The principal mediators of modulation are endogenous opioid compounds (endorphins and enkephalins). The primary site of action of these mediators is on the presynaptic membrane of nociceptors where up to 70% of their receptors are situated.Therefore ,they inhibit the pain signals before reaching the dorsal horn. Pain transmission is inhibited by opening of the K+ channels present on the nociceptor terminal.

ANTI-NOCICEPTIVE RECEPTORS – 2

Dynorphin activity is induced by Enkephelin in the spinal cord. Dynorphin causes GABA release by binding to receptors present in the inhibitory interneurons, that produces hyperpolarisation of the dorsal horn cells and inhibiting further transmission of pain.

INHIBITORY PATHWAY

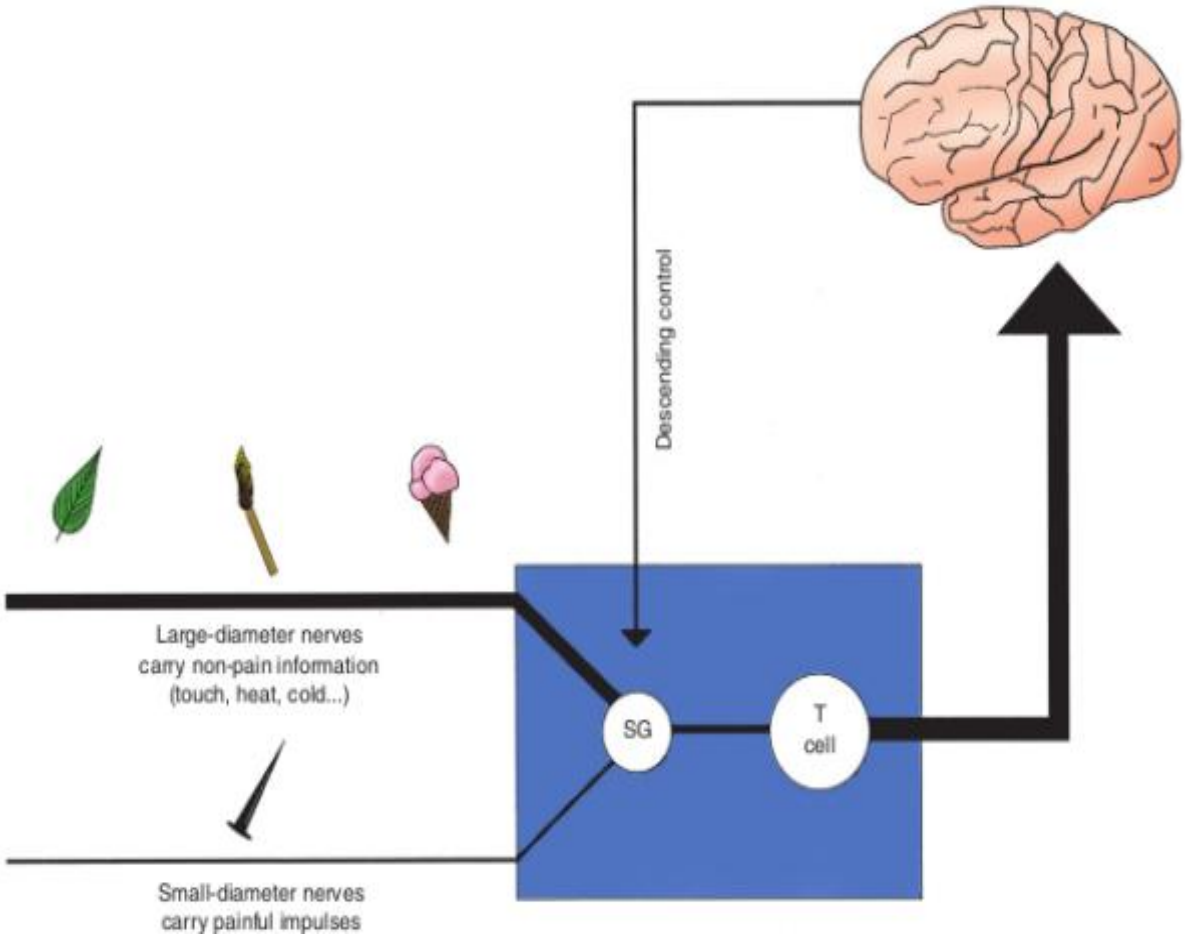
Transmission of pain can be inhibited at spinal and supraspinal level.

1**.SEGMENTAL INHIBITION**

Glycine and GABA are the important inhibitory neurotransmitters play an important role in the segmental inhibition. It is mainly mediated by the activation of GABA b receptor which increases the conduction of potassium across the membrane of the cell. Adenosine ,by stimulating ADENOSINE 1 receptor ,mediates its anti –nociceptive action.Activation of afferent fibres serving epicritic sensation inhibits WDR neurons and spinothalamic activity.

At the same time activation of noxious stimuli in non-contagious parts also inhibit WDR neurons .This explains GATE THEORY. (pain in one part inhibit pain in other part) **GATE CONTROL** theory of pain, by P. D. Wall and Ronald Melzack, it is a useful model about the physiological process of pain.

Gate control is one of the major pain theory. According to the gate control theory,



Pain is balanced between two informations, one through large fibers and other through small fibers in the spinal cord. In the absence of stimulation, both fibers are inactive and substantiagelatinosa is said to block the transmission of signal to the brain. The " gate is closed" and there is absence of pain.

With nociceptive stimuli, small nerve fibers are activated. They stimulate the transmitting cell neuros and inhibit the substantiagelatinosa, thus the inhibition of SG cell on transmission is overruled and pain occurs. The “gate is open”.That is pain is perceived whenever the substances that propagates pain impulse across “gate” in a nerve overrules the substances that tends to inhibit such an impulse.

2.SUPRASPINAL INHIBITION

Important site for these descending pathways include periaqueductal gray ,reticular formation and nucleus raphe magnus. These pathway mediate their anti-nociceptive action through alpha 2 adrenergic, serotonergic ,opiate receptors .Activation of these receptors ,activates second intracellular messengers,and causes opening of potassium channels and inhibits the increasing intracellular calcium concentration.Inhibitory adrenergic pathway mediate their action through nor-epinephrine.

Opiate system mediate their action through encephalins and beta endorphins. They act presynaptically and hyperpolarise primary afferent neurons and inhibit substance –p release

MISCONCEPTS ABOUT PAIN IN CHILDREN

MYTH	REALITY
1.Newborns and infants do not perceive pain. Children do not feel the pain as intense as adults because a child's nervous system is immature.	1. The anatomic and functional requirements for pain processing are present early in fetal life. As the descending pain control mechanism is immature in preterm infants and term newborns they are more sensitive to nociception.
2.Infants are incapable of expressing pain	2.we can assess behavioral and physiological cues that express pain in infants
3.Infants and children have no memory of pain.	3.it is noticed that preterm infants relate the alcohol smell with heel sticks and inorder to avoid it they pull out their legs away. Infants cry in anticipation immunizations.
4.Parents exaggerate or aggravate their child's pain	4.parents understand their child and can find out the pain in them
5.Children are not in pain if they can be distracted or if they are sleeping	5. Children use distraction to cope with pain, but they become exhausted soon by coping with pain

	and they fall asleep.
6.Repeated experience with pain teaches the child to be more tolerant of pain and cope with it better	6. Children with many experience in pain respond more intensely to pain. Experience with pain teaches them the severity of pain.
7.Children tolerate discomfort well. They become accustomed to pain afterhaving it for a while.	7. Children do not tolerate pain any better than adults. Infants may develop Sensitivity to pain with repeated exposure and tend to have a more pain reaction
8. Children recover more quickly than adults from painful experiences such as surgery.	8. Children heal quickly from surgery, but the severity of pain is similar to an adult
9.Children tell you if they are in pain. They do not need medication unless they appear to be in pain.	9.Children may be too young to express pain or afraid to tell anyone other than a parent about the same. The child may have fear that the treatment for pain is worse than the pain itself.
10. Children without obvious physical reasons for pain are unlikely to have pain.	10. The cause of pain cannot always be determined. The perception of pain is subjective and should be accepted by nurses.
11. Children run the risk of becoming addicted to pain medication when used for pain management	11. Addiction is extremely rare when treated for an acute condition it is less than 1%.

Physiologic Consequences of Unrelieved Pain in Children

Respiratory Changes

Includes rapid and shallow breathing which leads to respiratory alkalosis and expansion of lung id diminished which causes atelectasis.it is also associated with decrease in oxygen saturation, inability to cough leading to retention of secretions and infection.

Neurological Changes

Due to sympathetic overactivity there is release of catecholamines ,which causes increase in blood pressure,tachycardia,changes in mental status like irritability and insomnia.

Metabolic Changes

There is increase in the rate of metabolism with increased perspiration, elevated cortisol production.They can also be fluid and electrolyte imbalance and also causes altered blood glucose levels.

Immune System changes

Pain affects the immune and inflammatory responses and there by chance of infection risk and delay in wound healing is increased.

Gastrointestinal Changes

There is increase in the intestinal secretions and tone of the smooth muscle which causes anorexia, nausea and decrease in food intake .Mobility of the intestines are impaired which causes ileus.

Pain Response alteration

They can be increase in the sensitivity of pain sensitivity (Hyperalgesia) , threshold of pain is diminished and recall of painful experiences is accentuated.

CAUDAL ANAESTHESIA TECHNIQUE

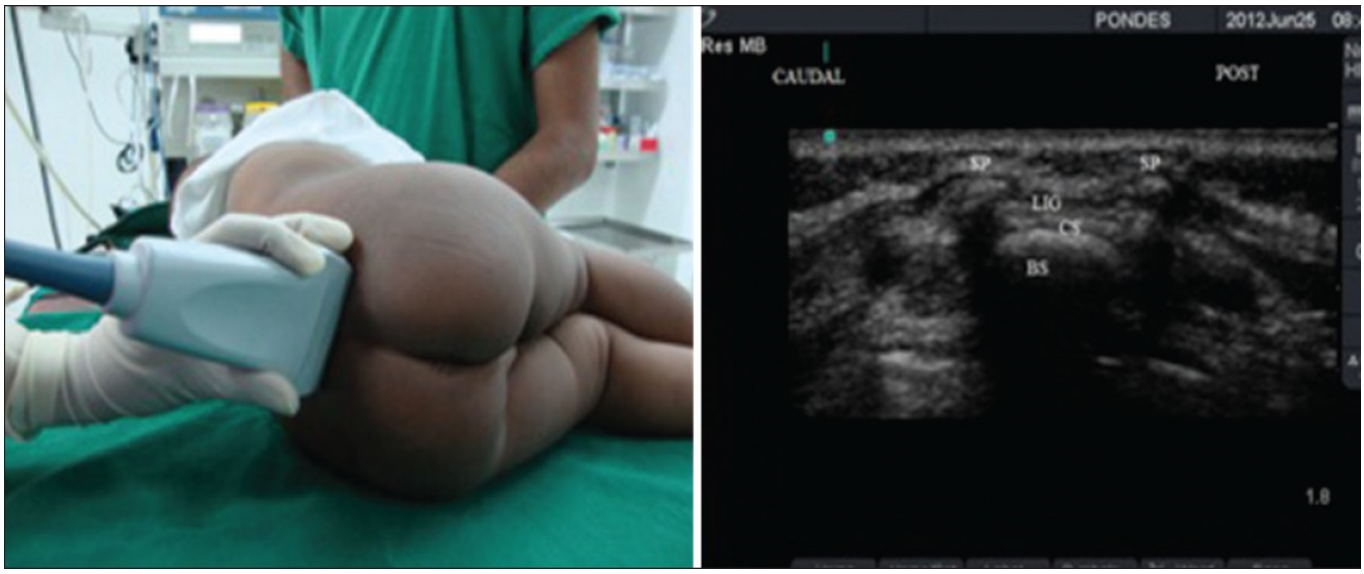
Caudal epidural sonoanatomy

The caudal space can be visualised in two views, transverse and longitudinal.

TRANSVERSE SCAN

The position of the probe

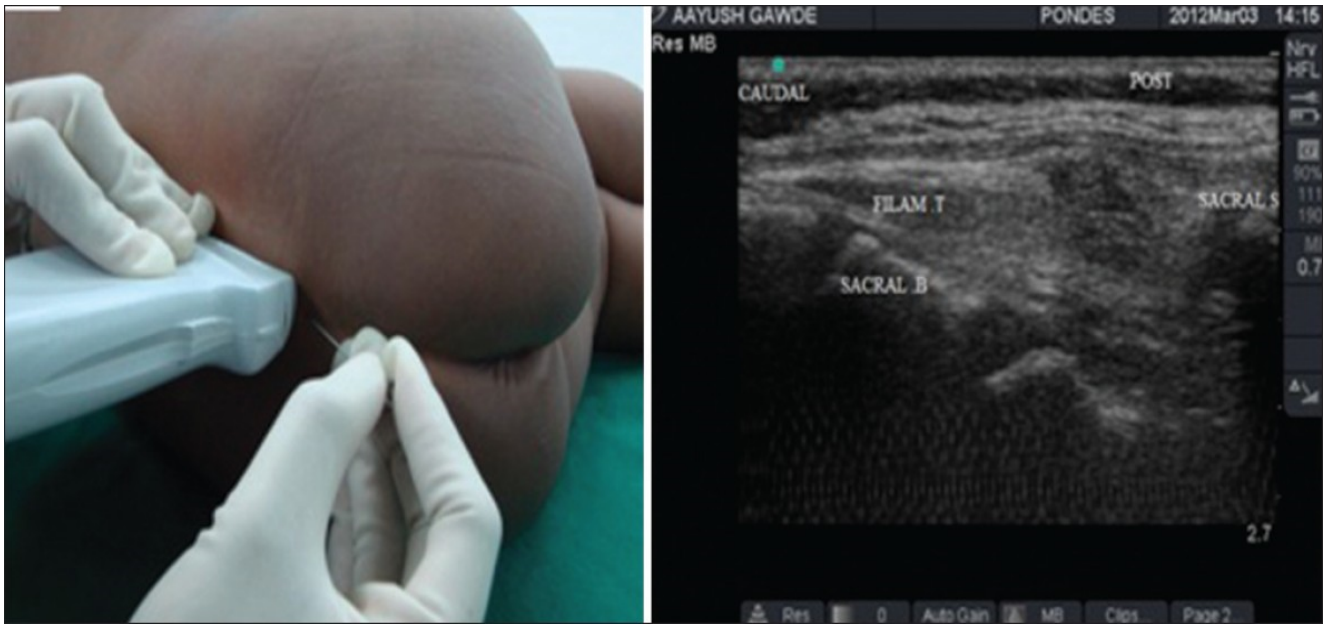
.



The scan shows two hyperechoic sacral cornua and dark acoustic shadows posterior to each of them. The hyperechoic fibrous structure intervening between them is the sacrococcygeal membrane or ligament. Posterior to the sacrococcygeal membrane is the base of the sacrum.

LONGITUDINAL SCAN

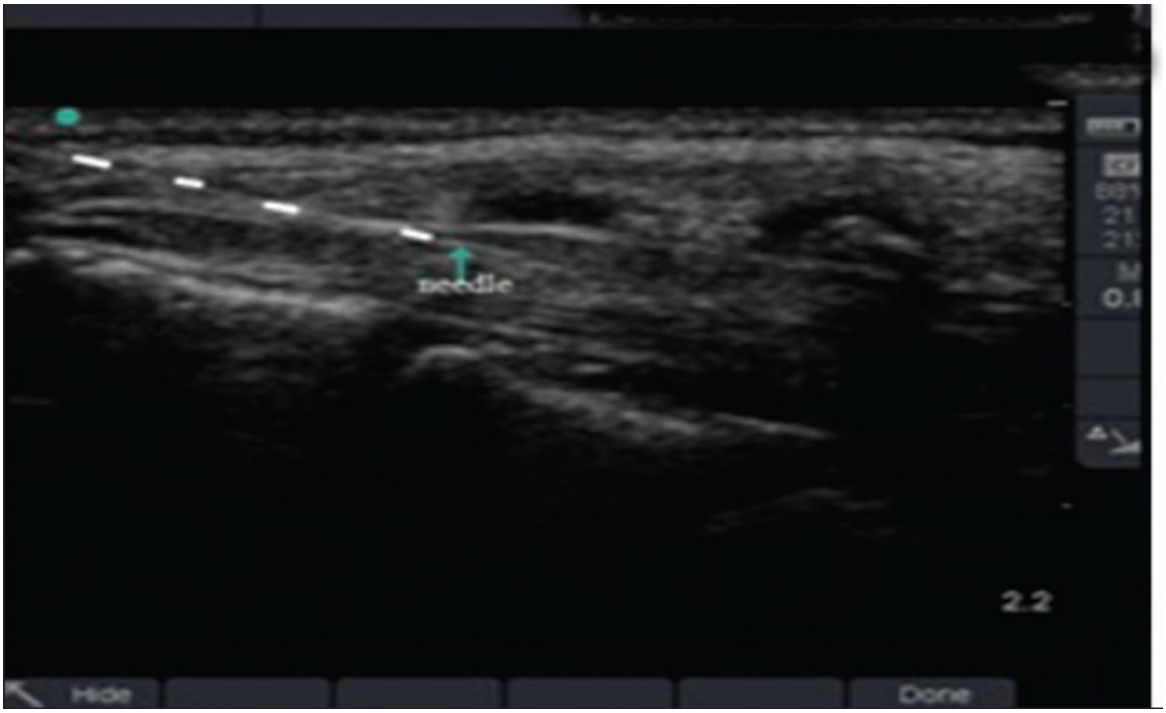
Position of the probe



The sacral vertebrae, the filumterminale and termination of the dural sac (conusmedullaris) can be identified in the longitudinal axis .Thefilumterminale is a cordlike hyperechoic structure and is surrounded by hyperechoic nerve roots of the caudaequina. It is difficult to differentiate filumterminale from the nerve roots due to their identical appearance (both appear like hypoechoeic structure.

NEEDLE PLACEMENT

The needle is inserted at an angle of 20-30° to the skin from the caudal space in an "in-plane" approach. After piercing the skin and subcutaneous tissue, it pierces the sacrococcygeal membrane to lie in the caudal spacehyperechoic strands



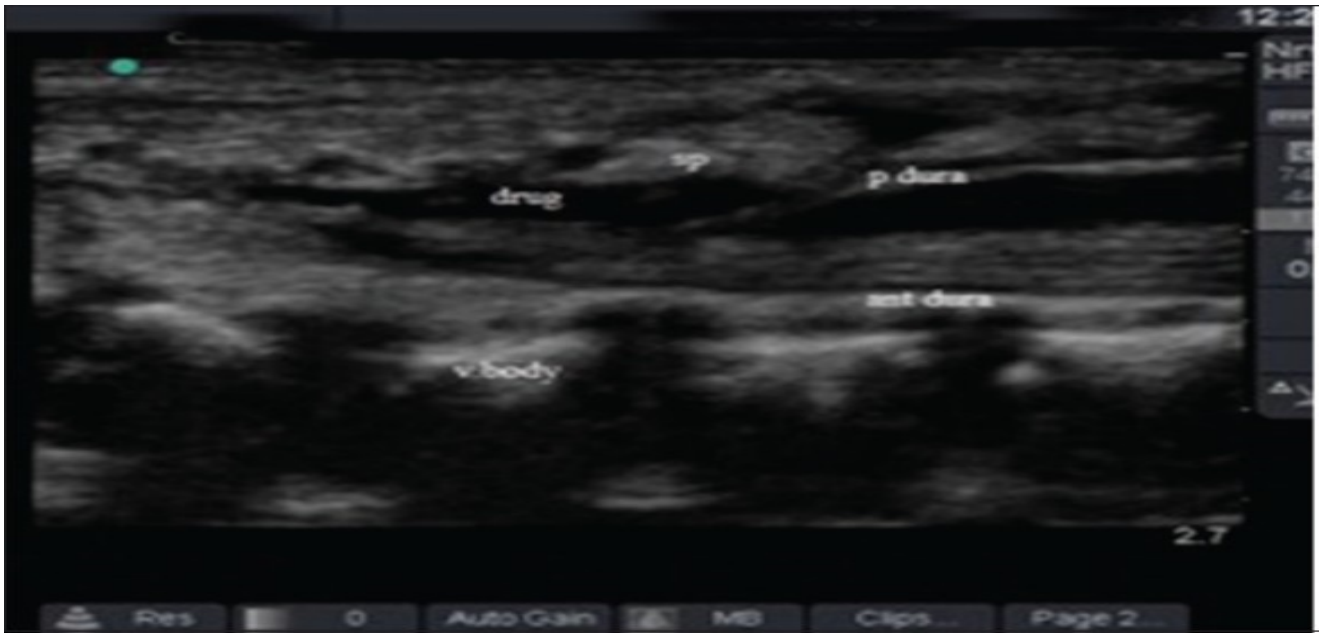
A needle placed well before (distal) the demarcation of conusmedullaris confirms the extradural placement of the needle. The subsequent complication such as a total spinal (due to injection of the drug in the CSF) is avoided.

LOCAL ANAESTHETIC INJECTION AND ITS SPREAD IN THE CAUDAL SPACE AS SEEN UNDER ULTRASOUND GUIDANCE

The observation of drug spread in the caudal epidural space has unveiled a lot of facts pertaining to its cranial spread. Posterior dural sag as the drug displaces posteriordura anteriorly while making its way in the cephalic direction is taken as a surrogate marker for correct drug placement.

The spread of the drug injected in the caudal block, two separate patterns were

observed: the horizontal intrasegmental redistribution from the dorsal to the ventral compartment of the epidural space and longitudinal caudal to cranial spread.



POSITIONING OF PATIENT

In adults , different positions can be used when compared with the lateral decubitus position in neonates and children. In children, due to the use of sedation prior to performing the block,airwaypreferred in children.

In children, blocks can be performed with the patient in fully anesthetized condition, but this is not needed for older children and adults. The most frequently utilized position in adults is prone position., but the lateral decubitus position or the knee-chest (also known as knee-elbow) position may be employed. In the prone position, there is a need for flexion of the procedure table or for producing slight flexion of the hips , a pillow may be placed beneath the

symphysis pubis and iliac crests .This position makes easily to palpate the caudal canal.

The legs are separated with the heels rotated outward to smooth out the upper part of the anal cleft while relaxing the gluteal muscles. In parturient, the lateral (Sim position) / knee-elbow position can be selected for performing caudal block.

INDICATIONS

1. Used in infra umbilical surgeries like repair of inguinal hernia,umbilicalhernia,orchidopexy,phimosis,anorectal and genitourinary surgery.

2. used in lower limb surgeries like pelvic or hip surgeries and for wound debridement of lower limbs.

3. It is indicated for lower limb surgeries especially in patients with neuromuscular diseases like muscle dystrophy.

4. It can be used as a sole anaesthetic technique in newborns and premature infants and thereby it avoids the risk of respiratory depression from residual muscle relaxants.

5. Can be used in malignant hyperthermia.

CONTRAINDICATIONS

1. Coagulation disorders

   Bleeding abnormalities like hemophilia,ITP,DIC or on anticoagulants such as heparin or Warfarin.

2. Infection

   Active cellulitis and pilonidal/perirectal abscess, and meningitis.

3. Hemodynamicinstability.Unstable blood pressure and/or heart rate

4. Parent refusal

5. Congenital anomalies of the spinal cord or vertebral bodies –like spina Bifida.

6. seizure disorders, meningomyelocele ,hydrocephalus.

COMPLICATIONS

TECHNICAL ERROR

1.SUB –CUTANEOUS INJECTION

There is 10 – 15% chances of vascular puncture,as epidural veins arevalveless ,intravascular injection produces arrhythmias ,hypotension and respiratory depression.Chance of dural puncture.

Remove the needle immediately if dural puncture occurs as it causes total spinal block.Intraosseous injection and penetration of sacrum.

2.COMPLETE OR PARTIAL BLOCK

Incidence is about 10 -25 %, common in children with anomalies like cloanalatresia,imperforate anus,Hypospadiasis and in older children.(>7 yrs old).

3.UNILATERAL BLOCK

Due to rapid injection of local anaesthetics, inadequate local anaesthetic volume. It occurs in 1 in 1000 cases.

4. epiduralhaematoma, epidural abscess.

5 .neurological complications like urinary retention occurs especially with narcotics.

6. nerve lesions are rare and other side effects like vomiting ,shivering , infection like meningitis.

7. poor psychological tolerance.

FACTORS DETERMING THE QUALITY OF BLOCK

1. type and concentration of local anaesthetic.
2. height of block which depends on the volume injected

Methods for determination of the volume of Local anaesthetic

Formula based on weight or age

ARMITAGE FORMULA

High sacral	- 0.5 ml /kg
High lumbar	-1 ml/kg
Thoracic level	-1.25 ml / kg

SCLHUTE – STEINBERG FORMULA (UP TO 8-12 YEARS)(1977)

0.1ml / segment / year

< 7 years – weight best predictor.Volume required in ml = 0.65 x number of segments to be blocked x body weight (kg)

SPIEGAL FORMULA

Total volume of injection (ml) = 4 + (D-15) / 2

Where D is the distance seperating the sacral hiatus from the spinous process of 7^{th} cervical vertebra.

MODIFIED SPIEGAL FORMULA

Volume of injection (ml) = 4 + (D-13) / 2

Despite larger volumes of local anaesthetic used in children as compared to adults, peak plasma levels of the local anaesthetics in children remain far below the toxic levels in adults.

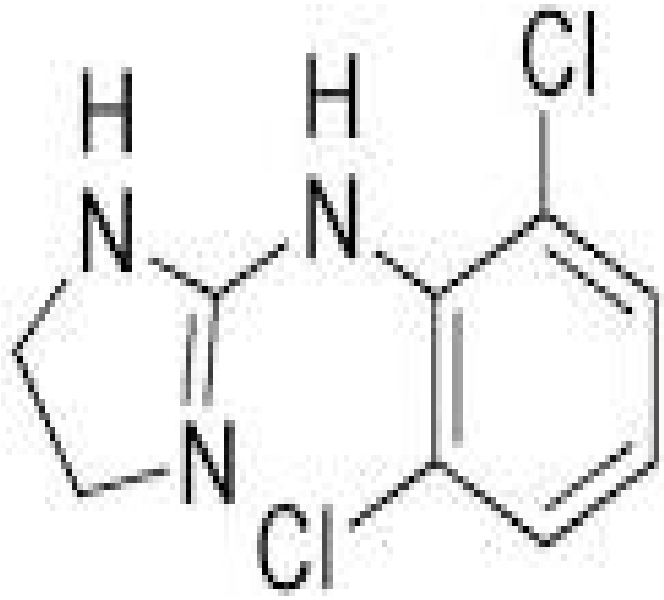
As the child grows, space becomes less compliant and large volume can cause higher spread of solution and thus increasing the concentration of local anaesthetics in the CSF.

PHARMACOLOGY

CLONIDINE HYDROCHLORIDE

In the year 1960,centrally acting partial alpha -2 agonist,clonidine hydrochloride was introduced.During its usage as a nasal decongestant ,its anti-hypertensive property was discovered.

It is an imidazoline compound and exists as mesomericcompound.Chemical name of clonidine is 2-(2,6 –dichlorophenylamino)-2 imidazole hydrochlorideC(H9C12HCL) is the structural formula of clonidine.



About 266.56 is the molecular weight of clonidine.Its physical characteristics are odourless in nature ,bitter in taste ,white in colour.

It is a crystalline substance and is soluble in alcohol and water,poorly soluble in acetone and chloroform.

Due to its sympatholytic effect ,it not only improves the quality of anaesthesia but also provides more cardiovascular stability during the intraoperative period. The anaesthetic agent dosage requirements decreases during anaesthesia.

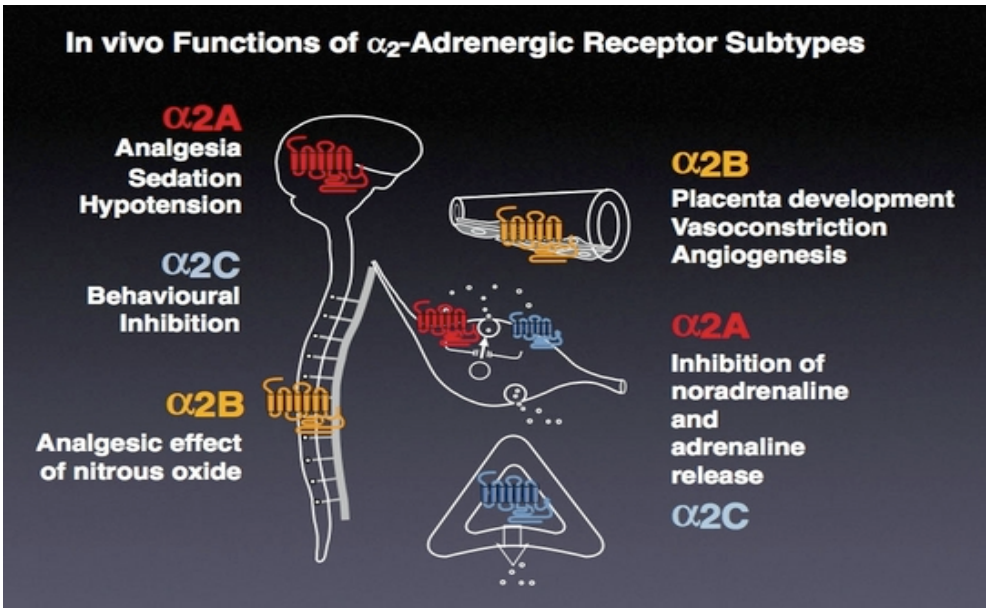
There is a 50% reduction in the MAC value of halothane in a dose dependent manner. In peripheral nerve blocks ,as well as in central neuraxial blockade clonidine prolongs the duration of action of local anaesthetics with less adverse effects.

Availability of clonidine

It is available in 1 ml ampule of about 150 microgram. The storage temperature of clonidine is below 25 degree Celsius.It is also available as tablets,transdermal patches.

MECHANISM OF ACTION

Clonidine is a centrally acting partial α2 adrenergic agonist .About 220: 1 is the sensitivity ratio of clonidine towards α 1 and α 2 receptors. This indicatessensitivity towards α2 receptors.



α2a,α2b,α2c are the three subunits of α2 receptors.The main action of α2a receptors are sedation, analgesia and sympatholysis.The main action of α2b receptors are anti- shivering and vasoconstriction. The activation of α2 c receptors mediates the startle response.

During epidural injection ,it crosses the blood brain barrier and reaches medulla and hypothalamus due to its lipid solubility.

Analgesic effects of clonidine are due to its direct suppression of neural transmission in the spinal neurons by activatingtheinhibitory α2 adrenoreceptors .Another effect of clonidine is the prevention of release of substance-P .

The α2 adrenoreceptors are located on the afferent terminals ofboth peripheral and spinal neurons in the superficial laminae of thespinal cord and with in several brain stem nuclei implicated in analgesia.

Three groups of neurons are present in the superficial laminae.They are tonic, adapting and single- spike firing neurons. They receives their primary sensory input from Aδ and C fibres.Analgesic effect of clonidine is due to its inhibition of voltage gated Na + and K + channels and thereby prevents action potential formation in the tonic spinal horn neurons.

Acetylcholine release may also contribute to the analgesic effect.Modificationof function of potassium channels in the CNS (cell membrane became hyperpolarized)by clonidine ,may be mechanism responsible for profound reduction in anaesthetic requirements. Clonidine also enhances analgesic effects of intraspinal opioids.

Clonidine acts on locus ceruleus and produces sedation. Due to its opposing action at different sites, blood pressure is affected in a complex manner after administration of drug via neuraxial or systemic route.

Due to the activation of post –synaptic α2 adrenoreceptors in locus cerelus and nucleus tractus solitarius of brainstem ,there is a decrease in the central sympathetic drive. In the lateral reticular nucleus ,it activates nor –adrenergic imidazoline binding sites and causes hypotension and anti-arrythmic effect.

Activation of presynaptic α2 receptors at the sympathetic terminals decreases the release of nor-adrenaline in the periphery and causes vasodialation and reduced chronotropic drive .The peripheral vasoconstriction effect through α2 adrenoreceptors nullifies the centrally reduced sympathetic drive.

The most desired effect of Clonidine is sedation and it producesin a dose dependent manner. At the dose od 50 micrograms or more,it produces sedation in less than 20 minutes irrespective of the route of administration.Even after massive overdose ,Clonidine doesn't produce profound respiratory depression. They doesn'tpotentiate respiratory depression due to opioids.

Due to the absence of α2 adrenoreceptors in the peripheral neuron axons , it causes minimal blockade at the peripheral nerves even at higher concentration. When added to local anaestheticsit enhances the peripheral nerve blockade probably due to its some effect on the C- fibres.

PHARMACOKINETICS

After oral administration it is absorbed rapidly. Its bioavailability is about 75-95%, within 60-90 minutes it reaches peak plasma concentration . The mean half life of the drug in plasma is about 9 to 12hours. About 20-40 % of the drug is bound to the plasma protein .

Approximately 50% of the drug is metabolized in the liver, whereas it is excreted in an unchanged form by the kidney. In impaired renal function ,thehalf life of clonidine is prolonged.

A transdermal delivery system is available in which the drug isreleased at a constant rate for about a week. Three of four days are required to achieve steady state concentration.A transdermal delivery system is available in which the drug is released at a constant rate for about a week.

300 micrograms intravenously over 10 min produces

Distribution t½ : 11± 9 minutes

Elimination t½ : 9± 2 hours, 41 hours in severeRenal dysfunction.

Volume of distribution : 2.1± 0.4 l/kg

Plasma protein binding : 20 - 40% in vitro

Metabolism : minor pathways with the major.

METABOLITE p – hydroxyclonidine.

EXCRETION

About 70 % of the parent drug is excreted unchanged in urine.So, depending upon the creatinine clearance, elimination t ½ of clonidine differs. About only 5 % of clonidine was removed from body store in hemodialysis patients.

Dosage regimen

Oral - 3-5µg/kg

Intramuscular - 2 µg/kg

Intravenous -1-3µg/kg

Spinal -50 -100µg

Epidural -1-2µg/kg

Transdermal - 0.1-0.3 mg released per day

PRECAUTIONS

1. In patients with renal insufficiency, lower dose is required.
2. Sudden withdrawal of prolonged continuous epidural infusion produces hypertensive crisis. So it should be gradually discontinued over 2 to 4 days.

3. Use with caution in patients with cerebrovascular or coronary insufficiency.
4. If a patient with beta blocker is on continous epidural therapy, beta blocker should be withdrawn several days before discontinuation of epidural clonidine.

CONTRAINDICATIONS

1. Known history of hypersensitivity to clonidine or any of its components .
2. brady arrhythmia or AV block
3. severe cardiovascular disease patients.
4. cardiovascular / hemodynamic instability.

INTERACTIONS

1. Clonidine may potentiate the CNS- depressive effect of alcohol, barbiturates or other sedative drugs.
2. Narcotics may potentiate the hypotensive effects of clonidine.
3. Tricyclic anti depressantslikephenothiazines and butyrophenonesmay antagonize the hypotensive effects of clonidine.
4. Concomitant administration of drugs with a negative chronotropicdromotropic effect (beta blocker, digoxin) can cause or potentiate bradycardiac rhythm disturbances.
5. Beta blockers may potentiate the hypertensive response seen with clonidine withdrawal.

6. Epidural clonidine may prolong the duration of pharmacologic effects of epidural local anaesthetics, opioids, neostigmine and other drugs.

USES

1. Pre anaestheticMedication : The dose of clonidine as preanaesthetic medications are 4mics/kg orally / nasally or 5mics/kg rectally. Eventhough the onset of sedative action was faster with midazolam than clonidine , but still clonidine has better patient satisfaction and sedation quality than midazolam. clonidine avoids midazolam effects like hallucinations and agitation. It is devoid of respiratory depression.clonidine taste is better than midazolam.clonidine causes sedation by sympatholysis and arousal to full consciousness is possible whereas in midazolam,patient have a state of cloudines of consciousness.

It avoids the sympatheteticoveractivity during intubation and prevents ,tachycardia ,hypertension and rise in intraocular pressure. It also prevents the release of catecholamines and cortisol in response to stress attenuation to surgery.

It also decrease postoperative adrenergic stress response and thereby reduces oxygen consumption.It also reduces intravenous and inhalational anaesthetic requirements.

1. Epidural block

Clonidine as sole agent or in combination withopioids or local anaesthetics to provide excellent analgesia inlabour analgesia. Epidural clonidine is also indicated for thetreatment intractable pain, which is unresponsive to maximumdoses of oral epidural opioid, as do patients with sympathetic dystrophy, neuropathic pain.

2. Spinal anaesthesia

Clonidine combined with local anaestheticsimproves the quality and duration of the block, minimize the tourniquepain during lower limb surgery, and preventsshivering.

3. Caudal anaesthesia

Clonidine combined with local anaestheticsincreases the duration of anaesthesia and analgesia by 2 or 3times without hemodynamic side effects Dose 2-3 µg/kg

4. Peripheral nerve blocks

Clonidine prolongs the duration ofanaesthesia and analgesia with local anaesthetics by two timesin a dose of 75 to 150 micro grams.

6. Bier's Block

150 microgram of clonidine enhances the tolerance of tourniquet.

7. It is also used in intra articular analgesia and also used in paediatric intensive care unit for sedation.

8. Protection against perioperative myocardial ischemia; clonidinedecreases myocardial ischemia, infarction and mortalityfollowing cardiovascular surgery.

9. To treat hypertensive crises and it also has antiemetic property.

10. Diagnosis of pheochromocytoma;0.3 mg will decrease the plasma concentrations of catecholamine in normal patients but not in the presence of pheochromocytoma.

11. Treatment ofshivering; Administration of clonidine,75 μg IVstops shivering by inhibit thermoregulatory control.

12. Treatment opioid and alcohol withdrawl syndrome

13 .It is used in the treatment of spasticity like cerebral palsy.

14. It decreases sevoflurane induced agitation and is also used in cyclical vomiting syndrome.

15. It is also used in sensory motor gating deficits like attention deficit hyperactivity disorder,post traumatic stress disorder ,schizophrenia due to its effect on the α 2c receptors.

SIDE EFFECTS OF CLONIDINE

1. sedation and xerostomia are the most common adverse effects.

2. Cardiovascular sideeffectsarebradycardia, hypotension, and EGG abnormalities like sinusnode arrest, junctional bradycardia; high degree AV block and arrhythmia are reported rarely. Occasionally bradycardiarequires treatment with I.V anticholinergics. Rarely orthostatic hypotension occurs .

3. Rebound hypertension: Occurs as early as 8hrs or late in 36hrs after the last dose. It is due to the abrupt discontinuation of clonidine and result in hypertensive crises.Symptomsincludesnervousness,diaphoresis,headache, abdominal pain, and tachycardia often precede the actual increase in systemic blood pressure. Labetalol is the treatment of choice of rebound hypertension.

4. frequently skin rashes occurs.

5. occasionaly ,there is incidence of Impotence .

6. It inhibits insulin release and increases blood glucose concentration.

OVER DOSAGE AND TREATMENT

For clonidineoverdosage ,there is no specific antidote available but often supportive measures like atropine, ephedrine, and i.v. fluids are satisfactory. Yohimbine partially reverses the analgesia and sedation but not the BP and heart rate changes produced by the epidural clonidine.Atipamezole can reverse the adverse effects of clonidine.

LOCAL ANAESTHETICS

These are the group of drug that causes reversible blockade of conduction of impulses along the nerve pathways . There is an interruption in the transmission of autonomic ,sensory and motor impulses and produces autonomic system blockade,sensoryanaesthesia, muscle paralysis.

CLASSIFICATION OF LOCAL ANAESTHETICS

Local anaesthetics have a hydrophobic aromatic group which is lipid soluble and a hydrophilic charged amide group. The drugs are classified into amide or esters group depending on the bond which connect the two groups.

ESTER GROUPS - Cocaine, chlorprocaine,tetracaine.

AMIDE GROUPS -Lignocaine,bupivacaine,prilocaine,benzocaine, mepivacaine,ropivacaine,levobupivacaine.

DIFFERENCES BETWEEN ESTERS AND AMIDES

AMIDES

They are more stable than ester group ,so it can be stored for long period.Allergic reactions are very rare.They are metabolized in the liver so it should be cautiously used in hepatic diseases.They diffuse through the tissues more rapidly than esters because of their lowerpKavalues.Toxicity chances are higher due to slow metabolism .

ESTERS

They are unstable in solution.They have higher pkavalue,so significantly more drug remains in the cationic poorly diffusible form at body pH.They are metabolized by plasmacholinesterasesintoparaaminobenzoicacid.(except cocaine which undergoes hepatic metabolism).So there is prolonged duration of action in atypical plasmacholinesterases.Allergic reactions are common mainly due to

its metabolite paraaminobenzoicacid.Toxicity chances are less as metabolism is faster.

ISOMERISM OF LOCAL ANAESTHETICS

Stereoisomerism may also be considered in local anaesthetics .it refers to existence of molecules with the same molecular and structural formula,with different spatial orientation around a chiral centre.

Bupivacaine is an example of stereoisomerism, as it has two stereoisomers, known as R and S forms. Another example is prilocaine whereas lignocaine and amethocaine are achiral.The combination of equal amounts of the two stereoisomers is called racemic mixture.The importance of these stereoisomers are they have difference in potency and side effects i.e.,levobupivacaine is less cardiotoxic.

PROPERTIES OF LOCAL ANAESTHETICS: depends upon

1. **LIPID SOLUBILITY**

   Onset and duration of action depends on lipid solubility. Potency of drug also depends upon lipid solubility. Highly lipid soluble drugs produce conduction blockade at lower concentration than less lipid soluble drugs because more molecule crosses the lipid barrier to reach the sodium channel. Duration of block is prolonged in highly lipid soluble local anaesthetics because they are less likely to be cleared by blood flow. Lipid solubility is measured in terms of partition coefficient between oil and

water. So local anaesthetic with high partition coefficient is more lipid soluble.

2. DISSOCIATION CONSTANT(pka)

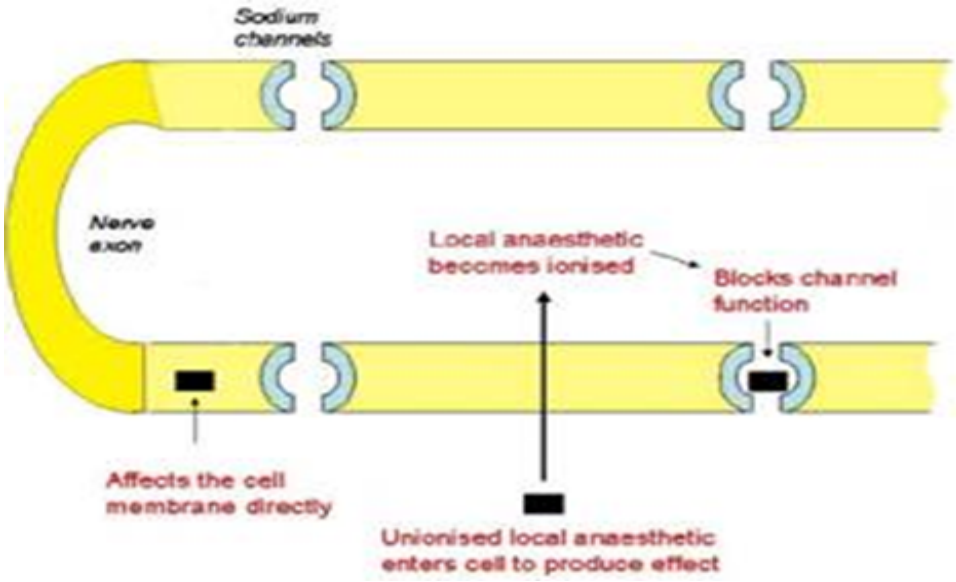
PKa is defined as pH at which 50% of drug in ionized form and 50% of drug in unionized form.

All the local anaesthetics have pKa>7.4. Any medium having pH <7.4 will be acidic for the drug. Acidic medium(sepsis) transfer more drug into ionized or non diffusible form. Drug with pKa more close to physiological pH will have more unionized form. That's why Lidocaine with pKa of 7.9 has faster onset of action than Bupivacaine with pKa of 8.1.

3. PROTEIN BINDING

Duration of local anaesthetics depends upon protein binding. Local anaesthetics with greater protein binding has longer binding with lipid sodium channel as it has protein spanning the bilayer cell membrane. It also binds to plasma proteins. Free drug concentration depends upon saturation with protein binding.

MECHANISM OF ACTION



Local anaesthetics block the sodium channel . on the inner portion of the sodium channel,there is a specific receptor for local anaesthetics. Local anaesthetics gain entry into their site of action through two mechanisms ,one is unionized(base) form penetrate their neuronal membrane due to their lipid solubility. Ionized(cationic form) reach the sodium channel directly through the external orifice.base form should be converted to cationic form before binding to the sodium channel.

THREE STATE OF SODIUM CHANNEL

Sodium channel has two gates ,one present intracellularly called inactivation gate (time dependent)and another present extracellularly called activation gate(voltage dependent) .

RESTING STATE

Activation gate closes and inactivation gate opens .

ACTIVATED STATE

During depolarization ,both gate opens ,there is inflow of sodium.

INACTIVATED STATE

Within few milliseconds, the inactivation gate closes after action potential and prevent the inflow of sodium channel.

CHARACTERISTIC OF BLOCKADE

1. It has no effect on the resting membrane potential.
2. It does not affect repolarization.
3. It is concentration dependent.
4. It produces reversible blockade.
5. It produces frequency –dependent blockade .,ie local anaesthetics selectively block nerves that fire frequently (sodium channel opens more number of times).

PHARMACOKINETICS

The rate of absorption of local anaesthetics,systemically depends upon the concentration of local anaesthetics, route of administration, total dose, vascularity of the injected areas and presence or absence of vasoconstrictors like epinephrine (1:200000) solution, presence of vasoconstrictors delays the absorption of local anaesthetics and reduces toxicity. Vasoconstrictors also

allows the usage of large doses of local anaesthetics.Other substances like sodium bicarbonate,hyaluronidase and opioids can be added to prolong the duration of action.

Placental transfer of local anaesthetics occurs by passive diffusion. Factors determining the rate and degree of diffusion are degree of plasma protein binding,degree of ionization and degree of lipid solubility.

Amide local anaesthetics are metabolized in the liver,hence patients with liver diseases are more prone to toxicity. Metabolites are excreted in urine, excretion depends on the urinary pH and urinary perfusion.

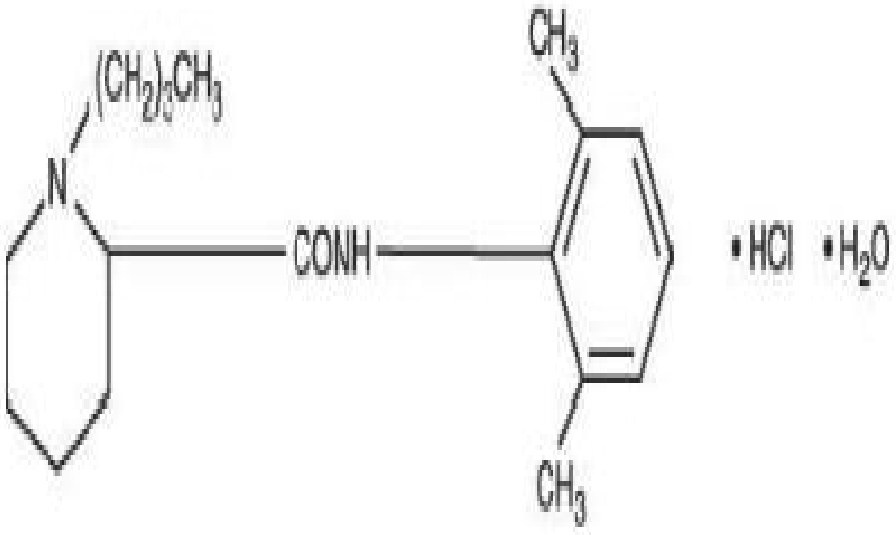
BUPIVAICAINE

It was first synthesized by EKENSTAM , in the year 1957.

Its chemical name is 1-butyl-2,6pipecoloxylidide hydrochloride .

It is a long acting amide local anaesthetics.

STRUCTURAL FORMULA



COMMERICAL PREPARATIONS

It is a white crystalline powder about 95% freely soluble in ethanol, it is soluble in water but slightly soluble in chloroform and acetone.

Bupivacaine is available as water soluble hydrochloride solutions with or without epinephrine (1:200000)bitartate.It is available in 0.25%,0.5%,0.75% concentrations. Epinephrine containing solutions need acidic pH,ascatecholamines are unstable in alkaline pH. Sodium bisulfite can be added to epinephrine solutions ,as it is strongly acidic.

MECHANISM OF ACTION

Local anaesthetics block the sodium channel and prevents the rise of action potential and thereby prevents the conduction as well as generation of nerve impulses. Blockade of nerve fibres depend on the diameter, myelination and conduction velocity of nerve fibres . Order of loss of nerve function are pain,temperature,touch,proprioception and skeletal muscle tone.

PHARMACOKINETICS

The drug is 95% protein bound , mainly with alpha1 acid glycoprotein, if the plasma protein binding sites are saturated or interfered with compounds like propranolol ,bilirubin,free drug level increases.

It undergo n-dealkylation in the liver to metabolites like pipecoloxylidine (major metabolite), N-desbutyl bupivacaine and 4-hydroxy bupivacaine.these metabolites are excreted in urine. About 6% of bupivacaine is excreted unchanged in urine, since bupivacaine is highly protein bound, it has low

fetal/maternal ratio(0.2-0.3) ,since placental transfer is inversely proportional to the protein binding. The onset of action is rapid and duration of action is prolonged, reaching the peak plasma concentration in about 30-45 min and decrease to insignificant levels in 3-6 hrs. Half life of bupivacaine is 2.7 hours.

USES

1. Used in central neuraxial blockade like spinal and epidural anaesthesia,peripheral nerve blocks,infiltration .
2. It has an anti-inflammatory effect and antibacterial effects.
3. It is also used in ophthalmic surgeries in the form of retrobulbar block.
4. Effective in labour analgesia, as it highly protein bound,placental transfer is minimal.
5. It inhibit neutrophil accumulation in the inflammatory sites and impair free radical release (prevents neutrophil priming).

SIDE EFFECTS OF LOCAL ANAESTHETICS

Principle side effects related to the use of local anaesthetics are due to the allergic reactions and systemic toxicity.

ALLERGIC REACTIONS

Usually allergic reactions to local anaesthetics are rare. It has been estimated that less than 1% of all adverse reaction to local anaesthetics are due to an allergic mechanism. Majority of adverse response that are often considered allergic response are due to excess plasma concentration of local anaesthetics.

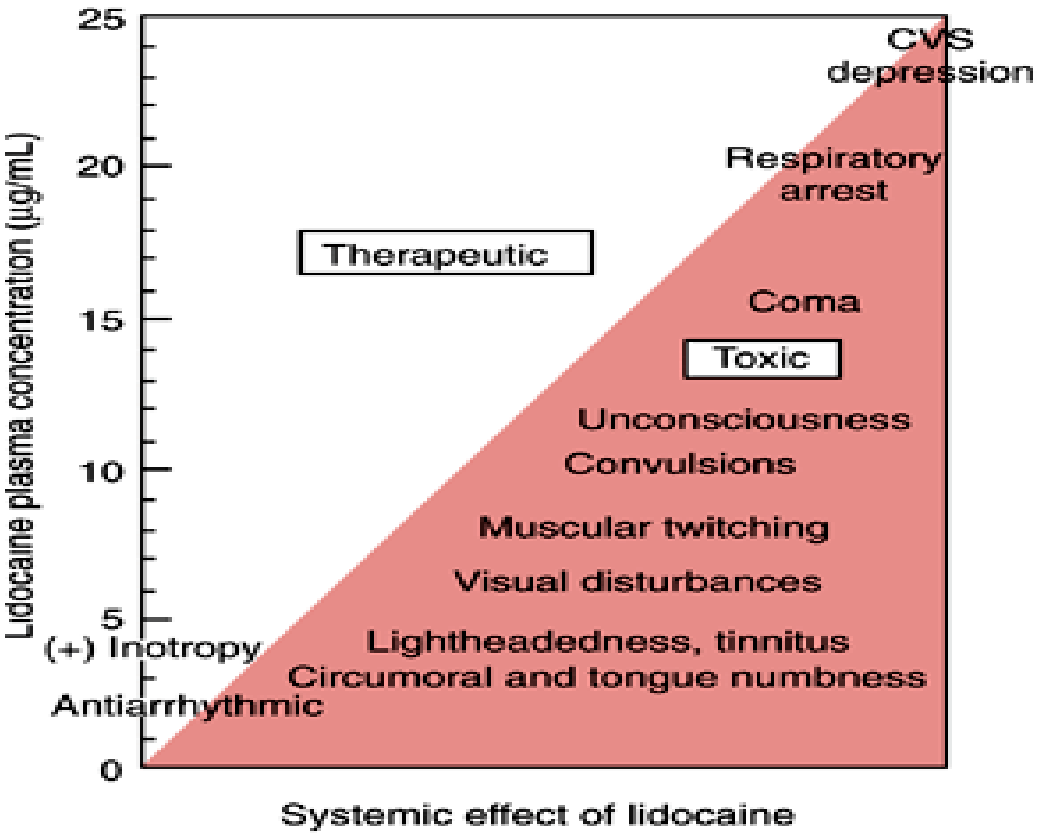
Allergic reactions after the use of local anesthetics may be due to methylparaben or similar substances used as preservative in commercial preparations of local anesthetics. Hence allergic reactions may reflect prior stimulation of antibody production to the preservative and not a reaction to local anaesthetics.

SYSTEMIC TOXICITY

Systemic concentration of local anaesthetics are due to excess plasma concentration. Plasma concentration of local anaesthetics can be determined by the rate of entrance of drug into the systemic circulation relative to their redistribution to inactive tissue sites and clearance by metabolism.

CNS

Low plasma concentration of local anaesthetics may cause numbness of tongue and circumoral tissues. As the plasma concentration continue to increase local anaesthetics readily crosses the blood brain barrier and produce the variety of cns changes initially such as breathlessness, tinnitus, difficulty in focusing. Further increase in cns concentration of local anaesthetics can cause slurred speech and skeletal muscle twitching is often evident in the face and extremities. And signals the imminence of tonic clonic seizures.



Seizures are then followed by cns depression and apnea.Onset of seizure reflect depression of inhibitory cortical neurons which leave the excitatory pathway unopposed.

Site of local anaesthetics induced seizures may be in temporal lobe and amygdala. The typical plasma concentration of bupivacaine associated with seizures is 4.5-5.5 mcgs/ml.

TRANSIENT RADICULAR RADIATION

This is mainly due to the irritation of lumbosacral nerves ,and is usually manifested as pain in the lower back , posterior thighs and buttocks .usually occurs with in 24 hours and lasts for 5-7 days . Incidence is dose dependent .0.5% bupivacaine or 0.5% tetracaine has lower incidence of transient radicular irritation than lignocaine.

CAUDA EQUINA SYNDROME

It was associated with the use of intrathecal lignocaine 5% and with the continuous use of intrathecal catheters . Mechanism was not clear ,it was thought due to the pooling of hyperbaric lignocaine causing direct neurotoxicity oif the cauda equine nerve roots and produces symptoms. The symptoms range from patchy sensory nerve deficits along the peripheral nerve distribution , motor deficits causing parasis of lower legs and can be associatwd with bladder and bowel disturbances.

ANTERIOR SPINAL ARTERY SYNDROME

This occurs due to the thrombosis of the anterior spinal artery which occurs due to the fracture of cervical spine or in hyperextension injury of cervical region. SPILLER was the first to describe anterior spinal artery syndrome.

Risk factors like pregnancy and postpartum induces hypercoagulable state. Clinical features are sudden lancinating pain ,paraesthesia , selective sensory loss of pain and temperature with preservation of tactile sensation and flaccid paralysis.

CARDIOVASCULAR SYSTEM

The main reason of cardiac toxicity of local anaesthetics is due to blockade of cardiac sodium channel. It also affect calcium and potassium channel and inhibit the production of cyclic monophosphate production (Camp).In higher plasma concentration the sodium channels are blocked so that conduction and automaticity become adversely depressed. It ,mainly affect the phase 4 of action potential of cardiac cells.

Intravascular injection of bupivacaine results in hypotension, cardiac dysarrythmias and atrioventricular block. After i.v injection of bupivacaine the protein binding sites are quickly saturated which leaves the significant mass of unbound drug available for diffusion into the conducting tissue of heart.epinephrine and phenylephrine may increase bupivacaine cardiotoxicity, reflecting bupivacaine induced inhibition of catecholamines – stimulated production of Camp.R -enantiomer of bupivacaine is more toxic than S-enantiomer.

Bupivacaine is more cardiotoxic than lignocaine , it is due to the order of avidity for displacing ligands from the beta adrenergic receptors. Larger molecules displace ligands at lower concentration ,because of this relationship between order of avidity and molecular size ,bupivacaine due to its large molecular size is more cardio toxic.

Plasma concentrations 5- 10 mics/ml of lidocaine causes hypotension . It is due to direct cardiac depression and because of the relaxation of the arterial smooth muscle ,it causes decrease in systemic vascular resistance and cardiac ouput.Cardio toxic effect of bupivacaine is due to its strong affinity towards sodium channel .it blocks the L –type calcium channel and sodium channel in cardiac cells and there by depress the conduction of impulses and cardiac contractility .Plasma concentrations of bupivacaine 0.5- 5 mics/ml causes cardiotoxicity.The changes in ECG are prolonged PR interval and QRS duration.

REVIEW OF LITERATURE

1. Jamali and colleagues conducted a study in the children of age group (1-7yrs)undergoing subumbilical and urological surgeries and they found that the mean duration of analgesia was increased in group with caudal bupivacaine o.25% plus clonidine 1mics /kg than the plain bupivacaine group .They also found that postoperative analgesic requirements also decreased in half of the clonidine received group,whereas about 13% of the children who receives only plain bupivacaine needed post operative analgesic requirement in the 24 hr period.

2. Cook and colleagues conducted a double blinded study in male children of age (1-7 yrs) undergoing orchidopexy , one group received caudal bupivacaine 0.25% (1ml/kg)with clonidine 2 mics/kg and other group received bupivacaine 0.25% (1ml/kg)with epinephrine 5 mics/ml.they found that time for rescue analgesia is prolonged in clonidine than epinephrine group with a mean of 5.8hr in clonidine group vs 3.2 hr in epinephrine group and p value of <0.05 and was significant.

3. Klimscha and colleagues conducted a study in children of ,mean age group 3yrs undergoing herniotomy.There were divided into three groups ,one group receives plain bupivacaine 0.25%(0.75ml/kg),second group receives caudal bupivacaine with clonidine 1mics/kg and third group receives bupivacaine with epinephrine (5mics/ml).They concluded that duration of

postoperative analgesia is increased as well as analgesic requirement were decreased in clonidine group than other two groups.

4. Motsch and colleagues conducted a study in children of age group 4-8 yrs undergoing minor surgery .They were divided into two groups with one group receives caudal bupivacaine 0.175%(1ml/kg) with clonidine 5 mics/kg .they found that the mean duration of postoperative analgesia was 20.9hrs with clonidine and is 14.4hrs with out clonidine group with a p value of <o.o5 and was significant.They also concluded tramadol requirement in the first 24 hrs increases in plain bupivacaine group than clonidine .only 3 children in clonidine group requires tramadol whereas 12 children in bupivacaine group receives tramadol.

5. Negri and colleagues conducted a study in children undergoing hernia repair or orchidopexy .They were divided into two groups ,with one group receives caudal ropivacaine0.2%(1ml/kg) and other group receives ropivacaine with caudal clonidine 2mics/kg and they concluded that mean duration of post operative analgesia was increased in clonidine group with a mean of 8.2hrs in clonidine group and 4.8 hrs in plain ropivacaine group. P value of <0.05 and was found to be significant.

6. Luz and colleagues conducted a study in children undergoing orchidopexy,hernia repair or circumcision.one group receives bupivacaine 0.18%(1.5ml/kg) with caudal clonidine (1mics/kg)and other group receives bupivacaine with caudal morphine (30 mics/kg).they reported that the mean

duration of analgesia was 6.3hr in clonidine vs 7.1 hr in morphine group with a p value of 0.43.

7. Sharpe et al conducted a study in children undergoing circumsion ,amd they compared between three groups, with one receiving bupivacaine alone ,second group receives bupivacaine with caudal clonidine 1mics/kg and three group with caudal clonidine 2 mics/kg and they concluded the duration of analgesia increases with increasing doses of clonidine.

8. El-hennaway and colleagues conducted a study in children undergoing lower abdominal surgeries and they divided children into two groups with one group receiving plain bupivacaine 0.25% (1ml/kg) with other receiving caudal clonidine 1mics/kg with bupivacaine 0.25% (1ml/kg) .They reported that duration of analgesia was prolonged in clonidine than bupivacaine with a mean of 12hrs in clonidine group.

9. R.singh , N.kumar and P. Singh (BJA 2010).They conducted a double blinded study in 50 children of age (1- 6)yrs undergoing upper abdominal surgeries .They were divided into two groups ,one group receives bupivacaine 0.25%(1.25ml/kg) with clonidine 2mics/kg and other group receives bupivacaine 0.25% (1.25ml/kg) with morphine 30mics/kg.They reported that caudal clonidine group has prolonged duration of analgesia with a mean of 16.5 hrsvs 10.2 hrs in morphine group with a p value of <0.01 and was significant and also clonidine group was without significant side effects.These studies conclude that caudal clonidine can also be used in upper abdominal surgeries also.

10. Hansen and colleague conducted a study in children undergoing sub-umbilical surgeries with three different concentrations of bupivacaine with clonidine 1mics/kg .one group receives o.125 %bupivacaine, second receives 0.25% bupivacaine and the last group receives 0.5% bupivacaine.they concluded that the action of clonidine depends on the concentration and volume of bupivacaine administrated caudally.They concluded that there is no benefit of adding clonidine to 0.125% bupivacaine .

11. Thomas R.Vetter et al conducted a study in children undergoing ureteral reimplantation.They were divided into two groups with one receiving caudal clonidine with ropivacaine and the other group receives ropivacaine with morphine and they reported that caudal clonidine was superior to caudal morphine .

12. Constant I .et al concluded a study to evaluate the benefits of adding clonidine or fentanyl to local anaethetics in caudal block in children.they reported that duration of surgical anaesthesia are prolonged as well as clonidine doesnot produce side effects compared to fentanyl.

13. T.G. Hansen ,S.W.Henneberg et al conducted a study in 46 children of age 1-5yrs undergoing hypospadias surgery. All children received general anaesthesia and Caudal block with bupivacaine 0.25%(0.5ml/kg).The children were divided into two groups ,with one group receiving clonidine 2mics/kg i.v and same amount of saline caudally and the second group receives clonidine 2 mics/kg caudally with same amount of saline i.v..they reported that mean

duration of analgesia was similar in both groups and concluded that clonidine whether administered caudally or intravenously had the same analgesic effect.

14. Abd –Elwahab , S.R .Boulis and etalconducted a study in 60 children undergoing lower abdominal surgeries .they were divided into three groups. One group received caudal bupivacaine 0.25% 1 ml/kg with clonidine 2microgram/kg.Second group received Bupivacaine 0.25% 1 ml/kg with Dexmedetomidine 2 microgram/kg. Third group received plain Bupivacaine0.25% 1ml/kg. They concluded that duration of analgesia prolonged with clonidine and dexmedetomidine group than plain bupivacaine group. But there was no significance in the duration of analgesia time between dexmedetomidine group and clonidine group. There was no significant hemodynamic changes or side effects between the groups.

15. Archanakoul et al conducted a study in 40children undergoing inguinal hernia repair and were divided into 2 groups randomnly, Group A received caudal bupivacaine 0.25% (0.75ml/kg) and clonidine 2 microgram/kg. Group B received 0.75 ml/kg of Bupivacaine 0.25% alone after induction of anesthesia. Postoperative duration of analgesia, observation pain scale, sedation score, heart rate and blood pressure were recorded. Duration of analgesia was significantly prolonged in group A (10.2hrs) than group B (4.55hrs) with a p value of <0.001 .Side effects like bradycardia, hypotension and sedation were not observed in Group A.

16. Hager et al conducted a study in 53 children of age 1-3 yrs undergoing hernia repair. They were divided into 3 groups ,with group 1 receiving caudal preservative free ketamine 1 mg /kg alone ,with group 2 receiving caudal ketamine with clonidine 1mics/kg and group 3 receiving caudal ketamine with clonidine 2 mics/kg. they reported that there is longer duration of analgesia with clonidine either 1mics/kg or clonidine 2mics/kg than ketamine alone.The analgesic requirement was only 16% in group 2 and 3 whereas it is 63% in Group 1.

17. Abdulatif et al conducted a study in 60 male children of age 2-10 yrs undergoing hypospadias surgery .they were divided into three groups ,group 1 receiving caudal 0.25% bupivacaine 1 ml/kg and group 2 receiving bupivacaine with neostigmine 2 mics/kg diluted in 0.9 % NACL solution to 1ml/kg . group 3 receiving neostigmine 2mics/kg alone caudally.they reported that mean duration of analgesia prolonged in group 2 than 1 and 3.

18. Bock and Kunz et al conducted a study in 80 children of age 3-8yrs receiving general anaesthesia with inhaled sevoflurane and caudal block with 0.175% bupivacaine 1ml/kg for minor surgeries.They were divided into four groups .,group -1 along with bupivacaine ,clonidine 1mics/kg is added, group -2 ., 3mics/kg added with caudal bupivacaine.,group -3 .,3 mics/kg clonidine given i.v., group -4., only caudal bupivacaine.they reported that clonidine 3 mics/kg

prevents agitation after sevofluraneanaesthesia independent of the route of administration.

19. Lee and etal conducted a study in 46 children of age 1-10 yrs undergoing orthoscopic surgery ,they were divided into 2 groups randomnly with group A receiving plain caudal bupivacaine 0.25% (1ml/kg) and group b receiving bupivacaine 0.25% with clonidine 2 mics/kg . the mean duration of analgesia was prolonged in group b (9.8hrs) than group A (5.2hrs) with a p Value of <0.0001 and there was no difference in side effects between the groups.

20. Akbas M et al conducted a study in children undergoing sub-umbilical surgeries. They compare the effects of caudal clonidine or ketamine when added to ropivacaine 0.25% (0.75ml/kg) had any effect on the stress hormone levels and the duration of caudal analgesia. They reported that clonidine group significantly prolonged the duration of analgesia as well as attenuate the stress hormone levels like glucose and corticol in response to surgery.

21. T.S.Yildiz et al conducted a study in 60 chidren of age 1- 10 yrs undergoing hernia repair surgery .They were divided into four groups .group 1 receiving plain caudal bupivacaine 0.125% (1ml/kg) ,group 2 - receiving bupivacaine 0.125%with clonidine 1mics/kg and group 3 receiving bupivacainewithclonidine 1.5mics/kg and group -4 receiving bupivacaine o.125% with clonidine 2 mics/kg.

They reported that duration of postoperative analgesia was significantly longer in clonidine 2mics/kg group with a mean of 650 mins.They also reported that there is no incidence of side effects like bradycardia and hypotension.

MATERIALS AND METHODS

A prospective randomized double blinded study was done to compare the effect of two different doses of clonidine with bupivacaine using ultrasound guided caudal block for post operative pain relief in children.After getting informed consent from the patient's parents ,this study was carried out in 50 children posted for infraumbilical surgeriesat Govt.Rajaji Hospital with a duration of (approx..30-60 min).The age group of these children are from 2-6yrs with the weight of 5-15kgs were selected for the study.

INCLUSION CRITERIA:

1. ASA I or II
2. Age- 2- 6yrs
3. Both sexes.

EXCLUSION CRITERIA

1. h/o allergy to local anaesthetics,
2. coagulation disorder.
3. spinal deformity like sacral abnormalities,spina bifida.
4. Any cardiac or neurological diseases.
5. local sepsis.

They were divided into 2 groups

Group 1 : 1ml/kg of 0.25% bupivacaine +1mics/kg of clonidine

Group 2 : 1ml/kg of 0.25% bupivacaine +2 mics/kg of clonidine

PREANAESTHETIC EVALUATION

1. Detailed history .
2. Examination of systems .
3. Investigations like hemoglobin, urine analysis.
4. Informed consent from parents .
5. Starvation status .

In the operation theatre ,monitors like pulse oximetry,NIBP were attached. Baseline values of parameters like MAP, PR, SPO2 were recorded.Iv line secured and ringer lactate werestartedas per calculated fluid requirements.

Premedicated with inj.atropine 0.02mg/kg,induction was done with standarised doses of inj.thio 5mg/kg and inj.fentanyl 2 mics/kg and inj.atracurium 0.5 mg/kg and intubatedwithappropriate size endotracheal tube.Maintained with 60%nitrous oxide and 40%oxygen and sevoflurane (1-2%).

Patients were positioned in left lateral position.-After aseptic precautions ,caudal space identified using Ultrasound and single shot caudal block was, performed with 23 G needle.

Group :1 patient receives clonidine 1mics/kg with bupivaicaine 0.25 % 1ml/kg.

Group :2 patient receives clonidine 2 mics/kg with bupivacaine o.25% 1ml/kg .

Technique of Needle placement using USG

Initially using transverse plane of imaging the sacral hiatus is identified

sacral hiatus is located between an upper hyperechoic line representing the sacrococcygeal membrane and an inferior hyperechoic line representing the dorsum of the pelvic surface (base) of the sacrum.

Rotate the probe longitudinally to capture the sacrococcygeal membrane , a relatively thick linear hyperechoicband,sloping caudally.

Insert the needle under longitudinal view which allows for optimal viewing along the needle. after placement with in the epidural space, spread of local anaesthetic is viewed as dilation of the caudal space and localized turbulence .

At the end of the operation,residual neurological blockade was reversed with appropriate doses of neostigmine and atropine, and extubated.

INTRAOPERATIVE MONITORING

Heart rate , MAP,SPO2 were recorded throughout the operation at an interval of five minutes.

Decrease in heart rate and MAP more than 30 % from the baseline values were treated accordingly.

POST OPERATIVE MONITORING

Heart rate and blood pressure were measured at 15, 30, 60, 90mins , 2hrs, 4hrs, 6hrs, 8hrs and 10 hrs postoperatively.

Assessment of pain by FLACC SCALE was done at 2, 6, 8, and 10 hours postoperatively.

The time of arrival to POCU to the first time when FLACC score was greater than 4 was noted as the duration of adequate caudal analgesia.

In FLACC SCALE , a score of 0 -2 was given ,with maximum of score 10.

0 - no pain.

1-3 - mild pain.

4-7 - moderate pain.

8-10 - severe pain.

FLACC SCALE

These are the following categories in flacc scale with score of 0-2.

category	0	1	2
face	No particular expression or smile	Occasional grimace,frown, disintersted	Frequent constant,clenchingjaw,quivered chin
legs	Normal position or relaxed	Restless,uneasy, tense.	Kicking or legs withdrawn.
activity	Lying quietly,normalposition,relaxed.	Squirming,tense, Shifting back and forth.	Arched ,rigid,steadily.
cry	No cry	Moans,whispers , occasional complaints.	Crying steadily or sobs,screams,frequently complaints.
Consolability	Content or relaxed	Reassured by occasional hugging,touching,or being touching distractable.	Difficult to console.

When the FLACC score was greater than 4 ,RESCUE ANALGESIA was given Paracetamol suppository was used as rescue medicine with a loading dose of 40 mg/kg followed by 20 mg/kg every six hours.

The number of doses of rescue analgesia and the time to which first rescue analgesia was given were recorded.

COMPLICATIONS

- vomiting,respiratorydepression,hypotension,bradycardia were also noted.
- Respiratory depression was defined as a decrease in oxygen saturation less than 93%, requiring oxygen by face mask.
- Hypotension was defined as systolic blood pressure less than 70 mm Hg
- bradycardia was defined as a heart rate less than 80 beats/min.

OBSERVATIONS AND RESULTS

Statistical Tools (To be included at the end of Materials and Methods)

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using Epidemiological Information Package (EPI 2010) developed by Centre for Disease Control, Atlanta.

Using this software range, frequencies, percentages, means, standard deviations, chi square, ‘t’ value and 'p' values were calculated. ‘t’ test was used to test the significance of difference between quantitative variables and Yate’s and Fisher’s chi square tests for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship

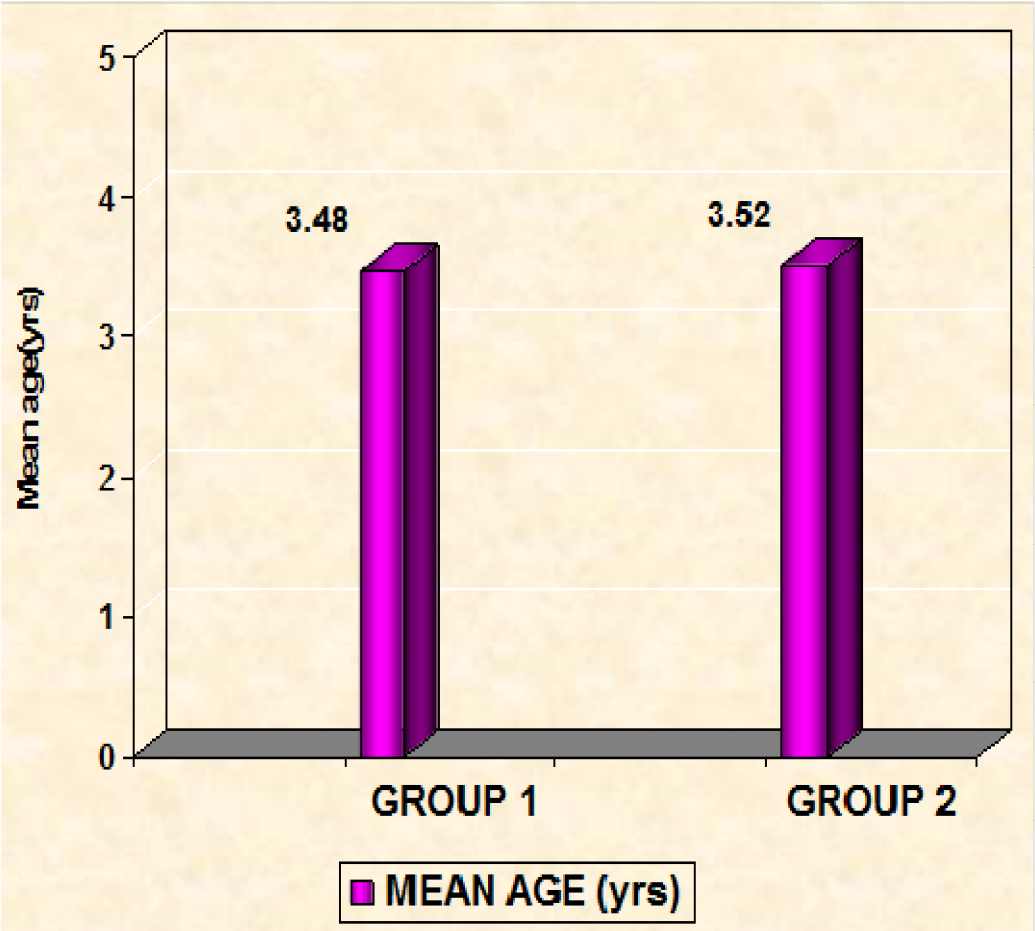
RESULTS

Table 1 :AGE

Group	Age (in year)		
	Range	**Mean**	**SD**
Group 1	2 - 6	3.48	1.12
Group 2	2 - 6	3.52	1.08
'p'	0.8986 Not Significant		

Age of the children between 2-6 yrs with the mean of 3.48 ± 1.12 in group 1 and 3.52 ± 1.08 in group 2 are comparable and statistically not significant.

AGE



The two groups were comparable in age .

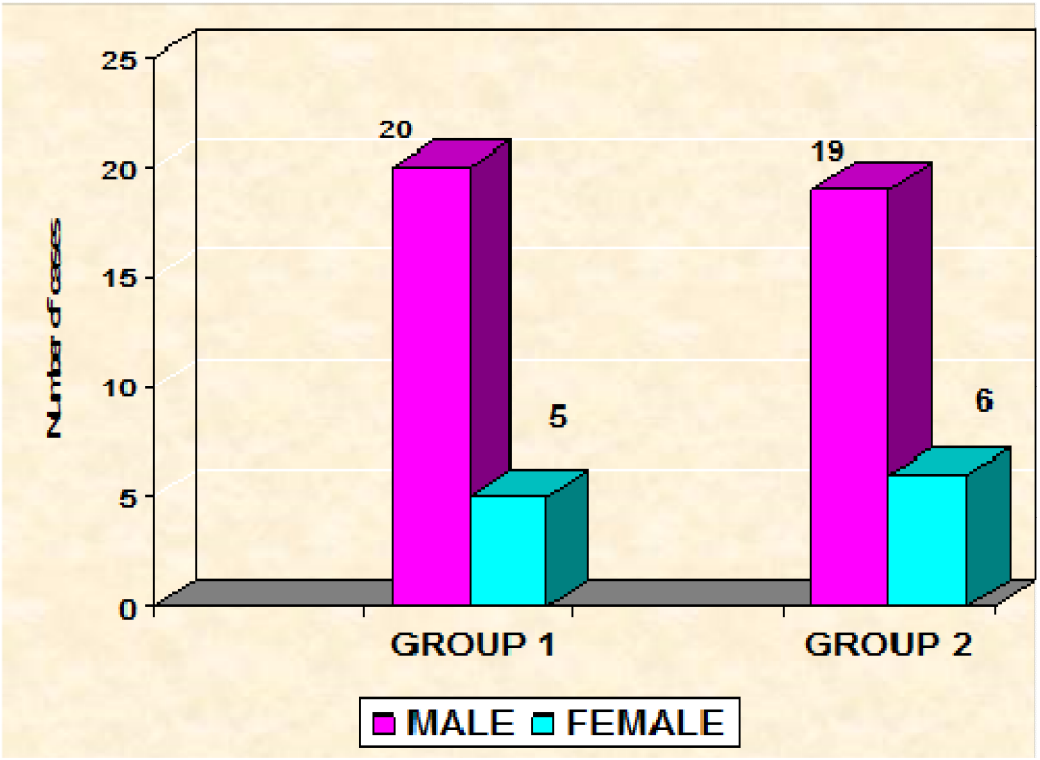
TABLE :2

SEX

Group	SEX			
	Male		Female	
	No	%	No	%
Group 1	20	80	5	20
Group 2	19	76	6	24
'p'	0.5 Not Significant			

Patients characteristics like sex were comparable and stastistically not significant.

SEX



This graph shows the two groups are comparable in sex.

Table 3 :WEIGHT

Group	Weight (in kg)		
	Range	**Mean**	**SD**
Group 1	5 - 20	11.32	3.4
Group 2	7 - 18	11.44	2.6
'p'	0.8163 Not Significant		

The table shows mean weight are comparable with mean of 11.8 ± 3.4 and 11.2 ± 2.6 in group 1 and group 2 respectively.

WEIGHT

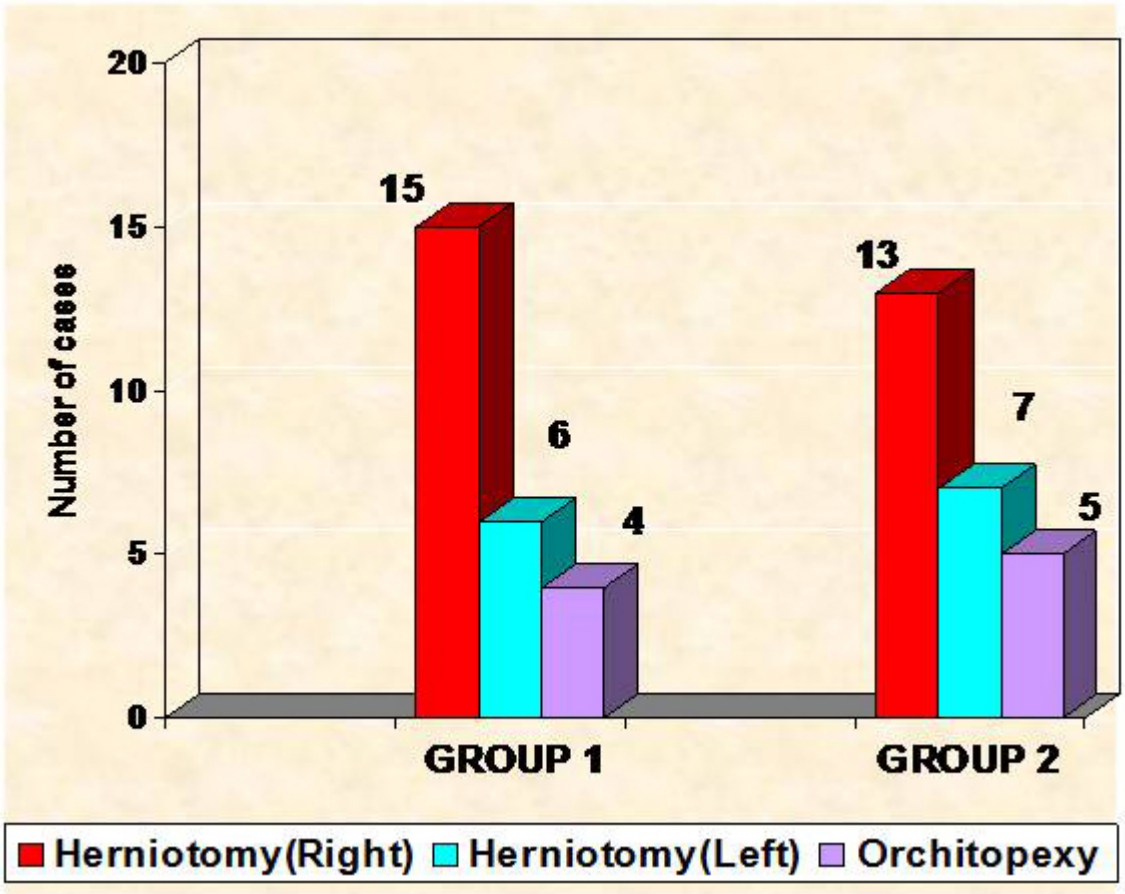
The graph shows mean weight are comparable with mean of 11.8 ± 3.4 and 11.2 ± 2.6 in group 1 and group 2 respectively.

Table 4 :TYPE OF SURGERY

Type of surgery	Group 1		Group 2	
	No	%	No	%
Herniotomy (Right)	15	60	13	52
Herniotomy (Left)	6	24	7	28
Orchidopexy	4	16	5	20
Total	25	100	25	100

The two groups were comparable in type of surgery.

TYPE OF SURGERY



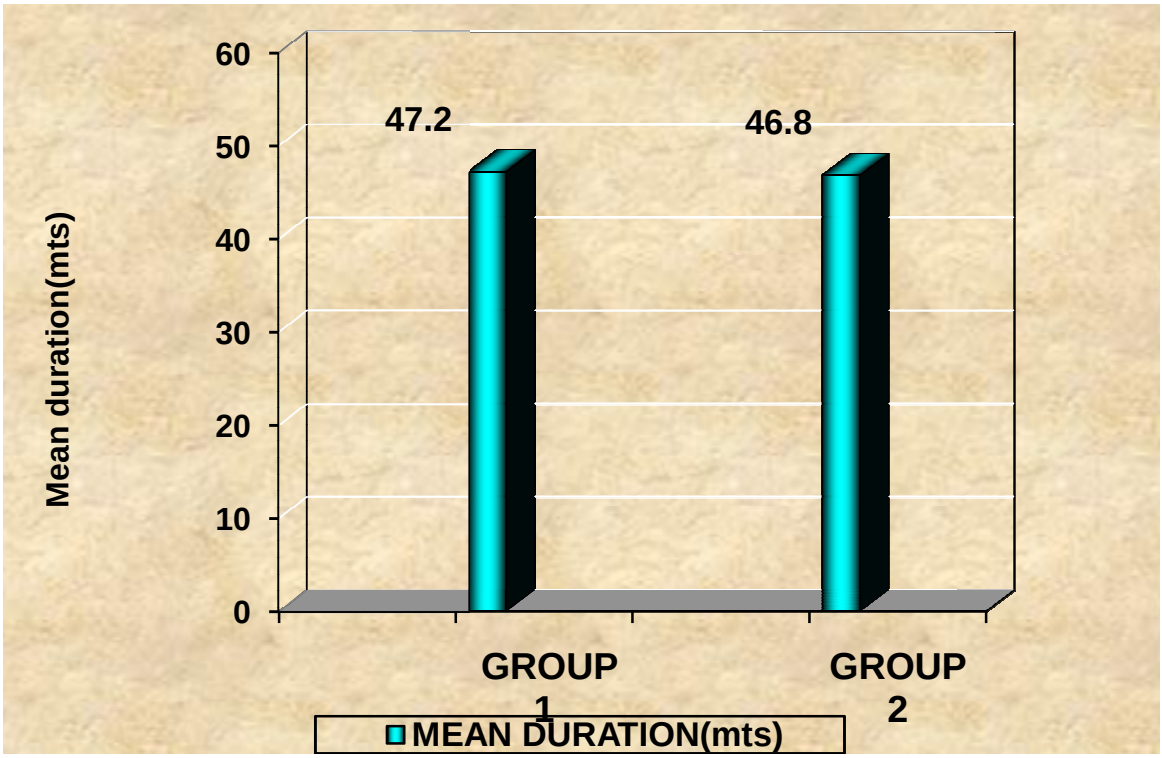
The two groups were comparable in type of surgery

Table 5 :DURATION OF SURGERY

Group	Duration of Surgery (minutes)		
	Range	**Mean**	**SD**
Group 1	30 - 60	47.2	9.4
Group 2	30 - 60	46.8	8.5
'p'	0.8752 Not Significant		

Duration of surgery in two groups were comparable with a mean of 47.2 ± 9.4 and46.8 ± 8.5 and statistically not significant.

DURATION OF SURGERY



Mean duration of surgery were comparable in both groups 1 and group 2 .

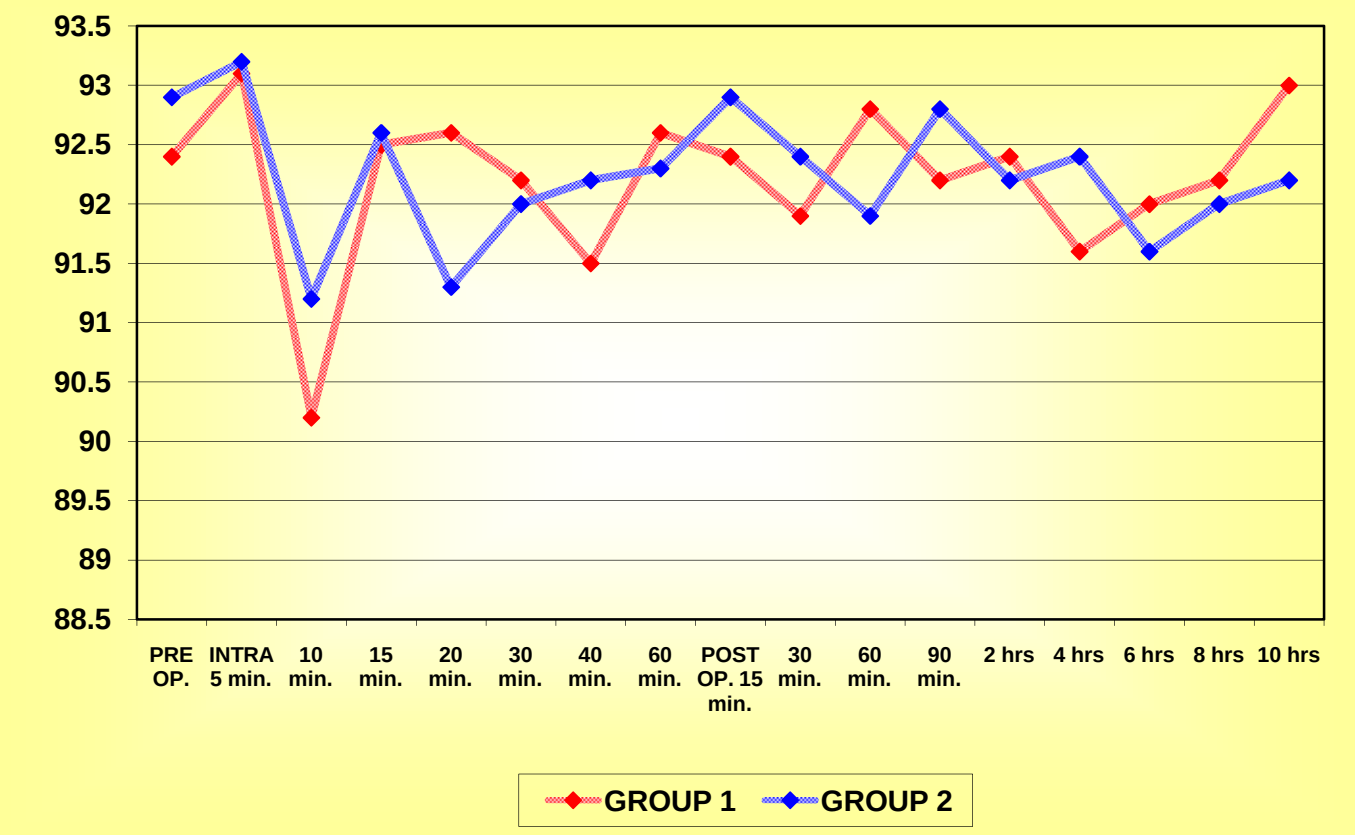
HEMODYNAMIC VARIABLES :

Table 6 :CHANGES IN PULSE RATE

Pulse Rate at	Pulse Rate of				'p'	Significant
	Group 1		Group 2			
	Mean	SD	Mean	SD		
Pre operative	92.4	4.6	92.9	3.1	0.6376	Not Significant
Intra Operative						
5 minute	93.1	2.3	93.2	2.2	0.8997	Not Significant
10 minute	90.2	3.4	91.2	1.9	0.2259	Not Significant
15 minute	92.5	2.6	92.6	2.1	0.9049	Not Significant
20 minute	92.6	2.2	91.3	2.0	0.0541	Not Significant
30 minute	92.2	2.0	92.0	1.6	0.5873	Not Significant
40 minute	91.5	2.6	92.2	1.4	0.2541	Not Significant
60 minute	92.6	2.6	92.3	1.1	0.624	Not Significant
Post operative						
15 minute	92.4	1.1	92.9	1.7	0.236	Not Significant
30 minute	91.9	1.1	92.4	1.1	0.0952	Not Significant
60 minute	92.8	1.2	91.9	1.1	0.0675	Not Significant
90 minute	92.2	1.2	92.8	1.2	0.0599	Not Significant
2 hour	92.4	1.6	92.2	1.2	0.55	Not Significant
4 hour	91.6	1.5	92.4	1.6	0.0873	Not Significant
6 hour	92.0	1.9	91.6	1.5	0.5119	Not Significant
8 hour	92.2	2.0	92.0	1.9	0.6641	Not Significant
10 hour	93.0	1.7	92.2	2.0	0.1371	Not Significant

Pulse rate was comparable between the two groups preop,intraop and postop.

PULSE RATE



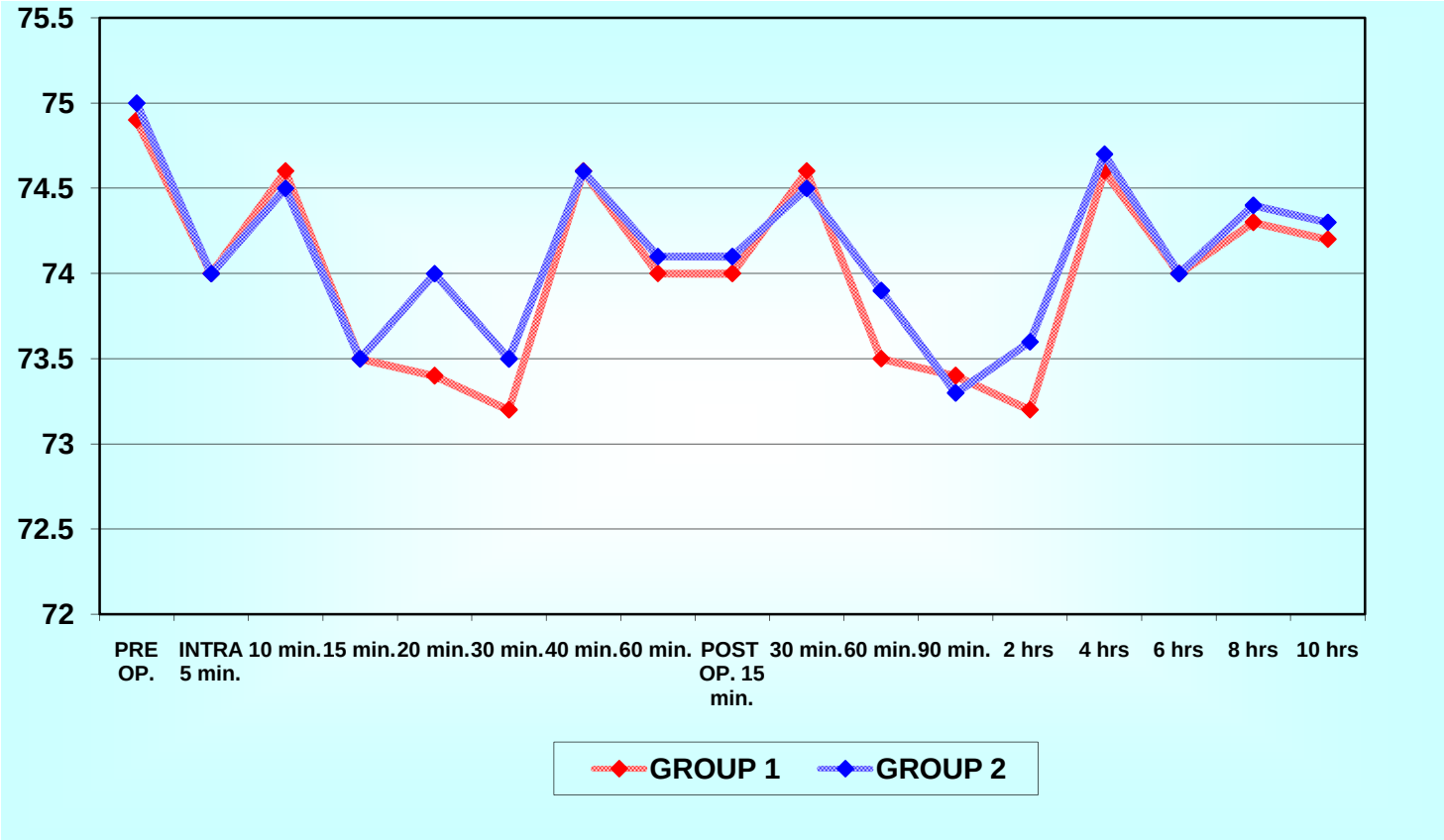
This graph shows no significant difference in pulse rate between the two groups pre op, intra op and post op.

Table 7 :CHANGES IN MEAN ARTERIAL PRESSURE

MAP at	MAP of				'p'	Significant
	Group 1		Group 2			
	Mean	SD	Mean	SD		
Pre operative	74.9	3.6	75.0	2.9	0.8971	Not Significant
Intra Operative						
5 minute	74.0	1.4	74.0	1.4	0.9212	Not Significant
10 minute	74.6	1.2	74.5	1.2	0.7305	Not Significant
15 minute	73.5	1.2	73.5	1.2	1.0	Not Significant
20 minute	73.4	1.3	74.0	1.4	0.1478	Not Significant
30 minute	73.2	1.2	73.5	1.3	0.3655	Not Significant
40 minute	74.6	1.6	74.6	1.7	0.8662	Not Significant
60 minute	74.0	1.0	74.1	1.3	0.7166	Not Significant
Post operative						
15 minute	74.0	1.4	74.1	1.3	0.8386	Not Significant
30 minute	74.6	1.2	74.5	1.2	0.7305	Not Significant
60 minute	73.5	1.2	73.9	1.2	0.2104	Not Significant
90 minute	73.4	1.3	73.3	1.3	0.7424	Not Significant
2 hour	73.2	1.2	73.6	0.8	0.1392	Not Significant
4 hour	74.6	1.6	74.7	1.6	0.93	Not Significant
6 hour	74.0	1.0	74.0	1.0	0.7827	Not Significant
8 hour	74.3	1.0	74.4	1.1	0.8937	Not Significant
10 hour	74.2	1.2	74.3	1.2	0.907	Not Significant

Both groups were comparable in MAP preop, intraop and postop.

MEAN ARTERIAL PRESSURE



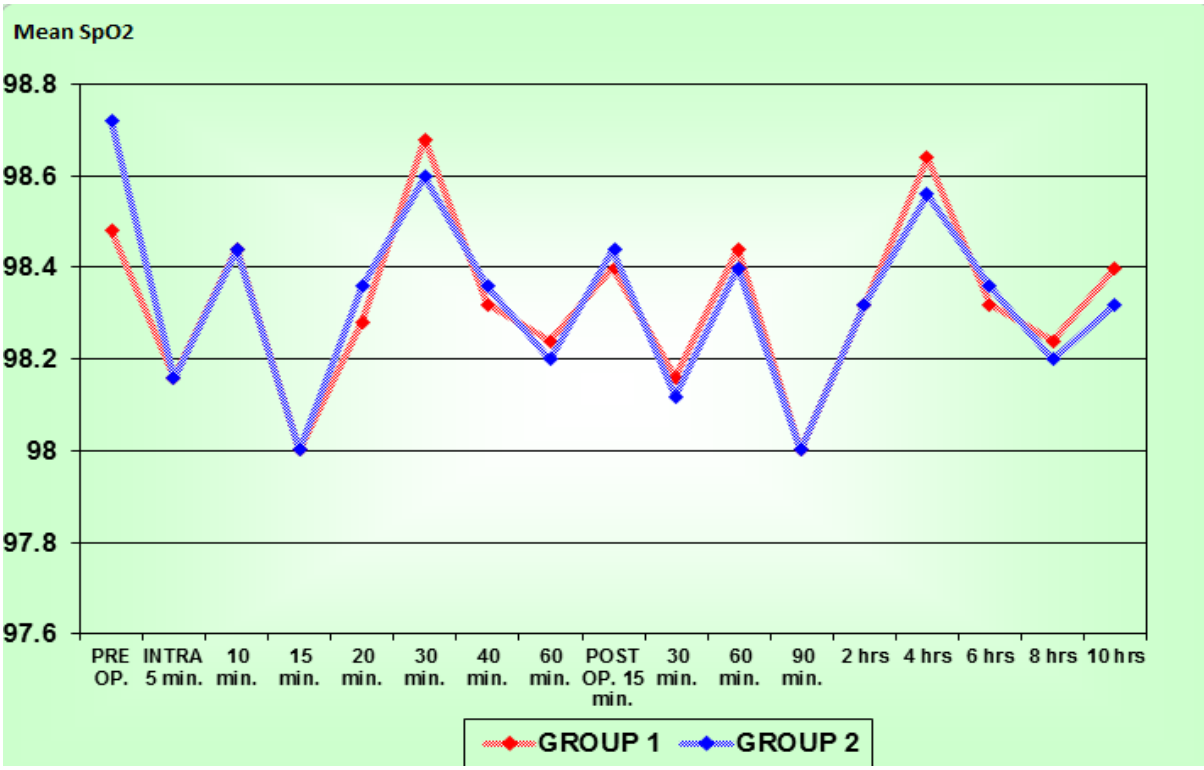
This graph shows no significant difference in mean arterial pressure between the two groups pre op, intra op and post op.

Table 8 :CHANGES IN SPO2

SPO2 at	SPO2 of				'p'	Significant
	Group 1		Group 2			
	Mean	SD	Mean	SD		
Pre operative	98.48	0.71	98.72	0.61	0.2087	Not Significant
Intra Operative						
5 minute	98.16	0.55	98.16	0.55	1.0	Not Significant
10 minute	98.44	0.51	98.44	0.51	1.0	Not Significant
15 minute	98.19	0.58	98.11	0.58	1.0	Not Significant
20 minute	98.28	0.54	98.36	0.57	0.6128	Not Significant
30 minute	98.68	0.48	98.65	0.5	0.5651	Not Significant
40 minute	98.32	0.69	98.36	0.7	0.8397	Not Significant
60 minute	98.24	0.6	98.23	0.58	0.8108	Not Significant
Post operative						
15 minute	98.4	0.58	98.44	0.58	0.8085	Not Significant
30 minute	98.16	0.55	98.12	0.53	0.7945	Not Significant
60 minute	98.44	0.51	98.4	0.58	0.7957	Not Significant
90 minute	98.0	0.58	98.0	0.58	1.0	Not Significant
2 hour	98.32	0.56	98.32	0.56	1.0	Not Significant
4 hour	98.64	0.49	98.56	0.58	0.6018	Not Significant
6 hour	98.32	0.69	98.36	0.7	0.8397	Not Significant
8 hour	98.24	0.6	98.2	0.58	0.8108	Not Significant
10 hour	98.4	0.5	98.32	0.63	0.6203	Not Significant

Two groups were comparable in mean spo2 during preop,intraop and postop.

SPO2



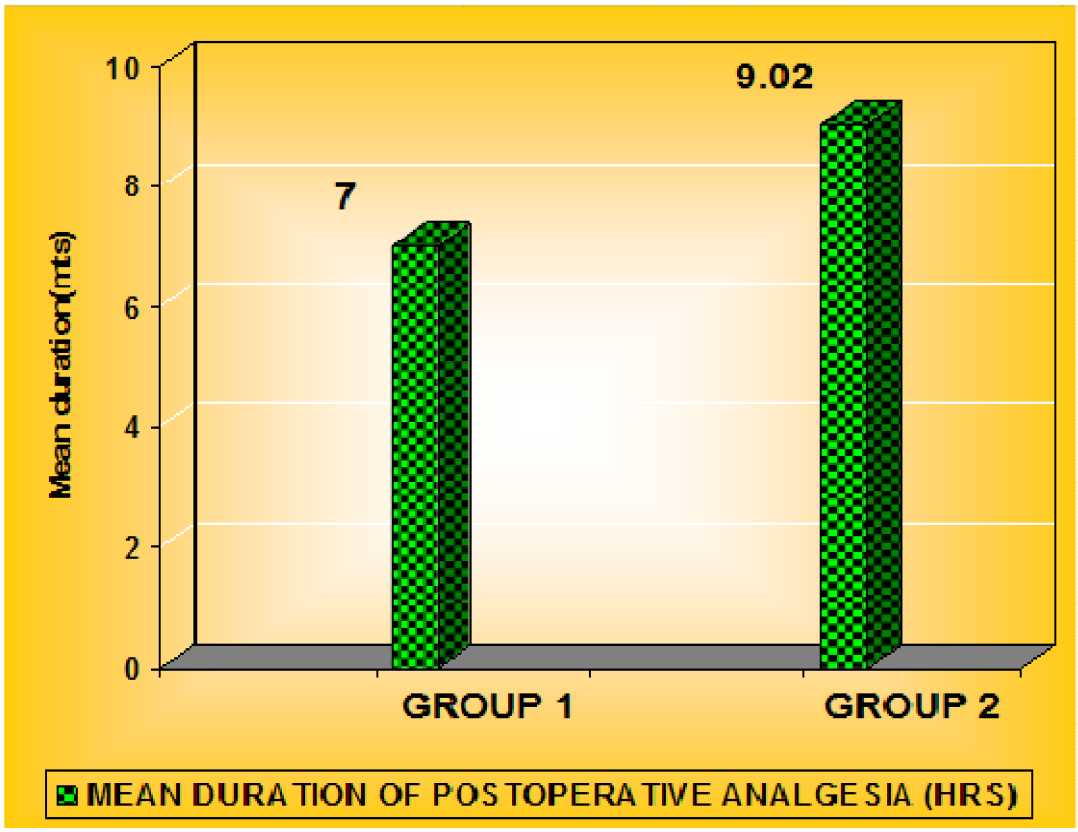
This graph shows no significant difference in SPO2 between the two groups pre op, intra op and post op.

Table 9 :DURATION OF POST OPERATIVE ANALGESIA

Group	Duration of Post Operative Analgesia (hours)		
	Range	**Mean**	**SD**
Group 1	5.5 - 8	7.0	0.71
Group 2	8 - 10	9.02	0.55
'p'	**<0.0001 Significant**		

The mean duration of post op analgesia between the group 1 and group 2 are 7 ± 0.71hrs and 9.02 ± 0.55hrs and is found to be statistically significant with the p value of < 0.0001.

DURATION OF POST OPERATIVE ANALGESIA



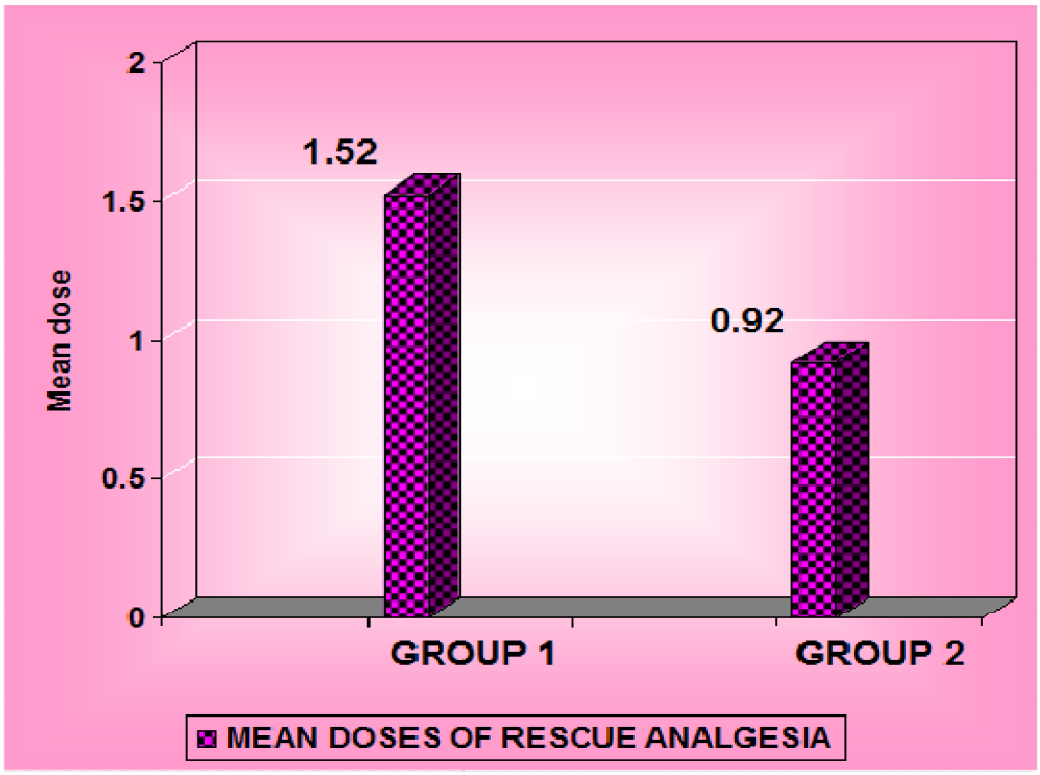
The mean duration of post op analgesia between the group 1 and group 2 are 7 ± 0.71hrs and 9.02 ± 0.55hrs and is found to be statistically significant with the p value of < 0.0001.

Table 11 :NUMBER OF DOSES OF RESCUE ANALGESIA .

Doses of Rescue Analgesia	Group 1		Group 2	
	No	%	No	%
0	4	16	10	40
1	10	40	8	32
2	5	20	6	24
3	6	24	1	4
Mean SD	1.52 1.05		0.92 0.91	
'p'	**0.0354 Significant**			

The number of doses Rescue analgesia between the group 1 and group 2 are 1.52 ± 0.92 and 1.05 ± 0.91 and is found to be statistically significant with the p value of < 0.0354.

NUMBER OF DOSES OF RESCUE ANALGESIA



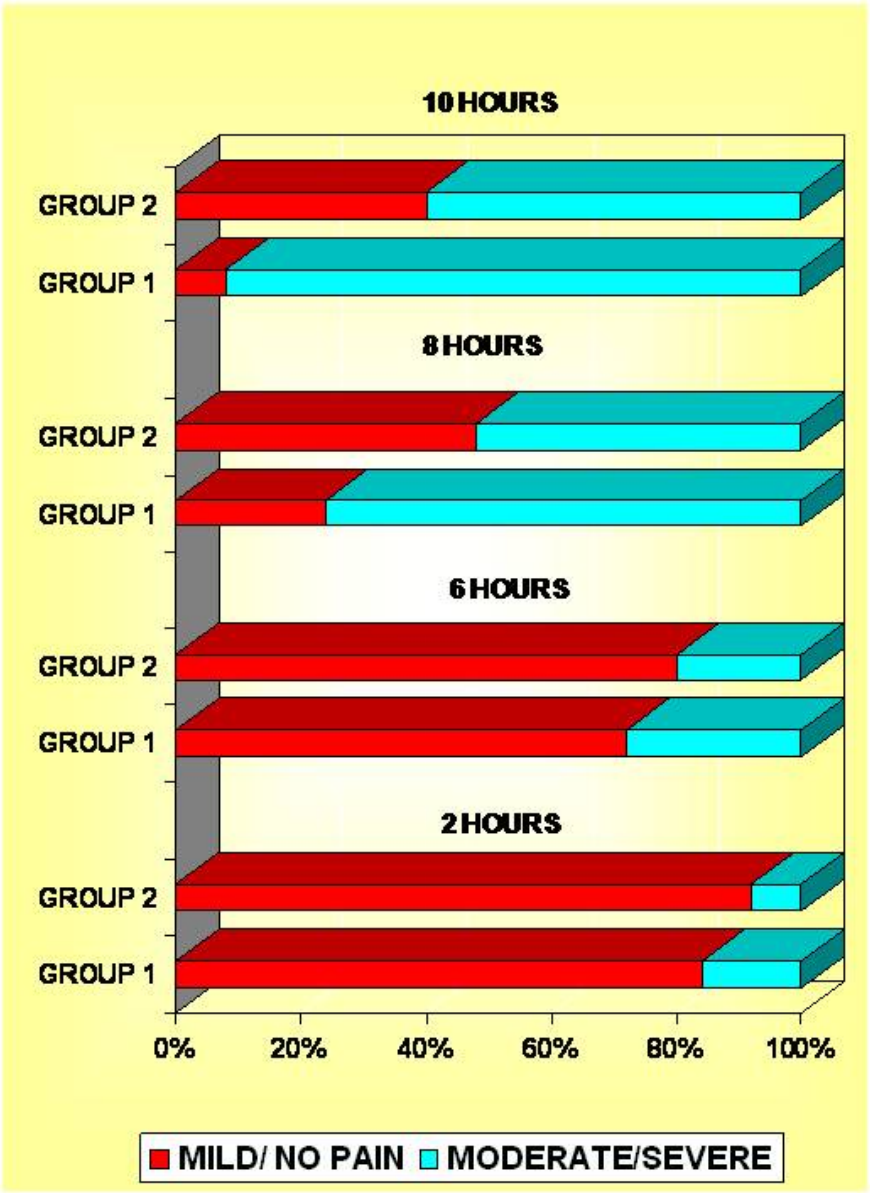
The no of doses Rescue analgesia between the group 1 and group 2 are 1.52 ± 0.92 and 1.05 ± 0.91 and is found to be statistically significant with the p value of < 0.0354.

Table 12 : FLACC PAIN SCALE

FLACC Pain Scale		**Group 1**		**Group 2**		**'p'**
At	Score	**No**	**%**	**No**	**%**	
2 hours	Mild / No pain	21	84	23	92	0.3336 Not Significant
	Moderate / severe	4	16	2	8	
6 hours	Mild / No pain	18	72	20	80	0.3708 Not Significant
	Moderate / severe	7	28	5	20	
8 hours	Mild / No pain	6	24	12	48	0.0699 Not Significant
	Moderate / severe	19	76	13	52	
10 hours	Mild / No pain	2	8	10	40	**0.009 Significant**
	Moderate / severe	23	92	15	60	

FLACC SCALE was found to be significant between group 1 and group 2 at 10 hrs with a p value of 0.009

FLACC PAIN SCALE



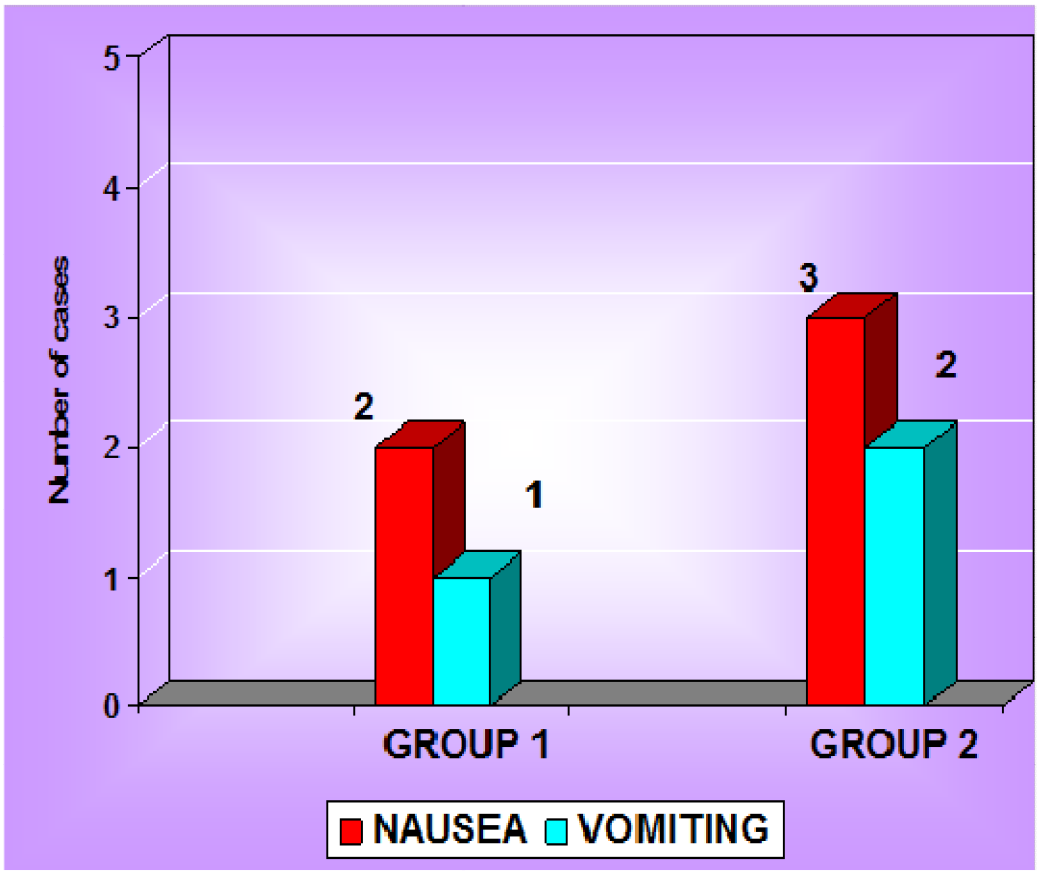
This graph shows significant difference in FLACC scale score at 10 hours between the two groups .

Table 10 :COMPLICATIONS

Complications	No. present in				'p'
	Male		Female		
	No	%	No	%	
Nausea	2	8	3	12	0.5 Not Significant
Vomiting	1	4	2	8	0.5 Not Significant
Hypotension	-	-	-	-	-
Respiratory Depression	-	-	-	-	-
Bradycardia	-	-	-	-	-

None of the case has bradycardia or hypotension.

COMPLICATIONS



Graph shows the incidence of nausea and vomiting.

DISCUSSION

Caudal analgesia remains unique in the cornerstone of paediatricanaesthesia for providing analgesia in the intraoperative and post operative period , especially in children undergoing perineal,infra umbilical and lower extremity surgery.

VirushaliChandrashekharPonde(Indian Journal ofAnaesthesia 2012) in his review article ,quoted about recent advances and development in paediatric central neuraxialanaesthesia such as use of ultrasound guidance and electrical stimulation . The correct needle placement in electrical stimulation is indicated by contraction of anal sphincter.

These advancement upgrade neuraxial block still effective and safer. Eventhough caudal block is very simple technique ,it also has its own complications like intraosseous,intravascular and intrathecal.Conventional or blind technique is assessed by loss of resistance technique which is subjective variable.Use of ultrasound or electrical stimulation confirms the correct needle placement which avoids blind injury to bony structures .

In this study caudal block was performed under ultrasound guidance.

Among the drugs used for caudal block ,Bupivacaine remains the local anaestheticused mostcommonly,ropivacaine which is similar to bupivacaine but has less motor blockade is being used extensively.Manyaddictives have been added with bupivacaine to increase its duration of action .Adjuvants like ketamine which is preservative free, morphine,fentanyl, clonidine , midazolam ,dexmedetomidine ,epinephrine have been added.

We in this study combined clonidine with bupivacaine , clonidine was selected as it offers many advantages over opioids . clonidine is a selective α2 agonists. Clonidine decreases central sympathetic drive by stimulating the inhibitory α2 receptors and decrease the nor- adrenaline release ,thissympatholysis will reduce intraoperative requirements of analgesics and inhalational anaesthetics.

Sympatholysis effect causes sedation, where child can be aroused to full consciousness. It is alsodevoid of respiratory depression, pruritis and urinary retention which is seen with opioids.

CLONIDINE analgesic effect is due to its suppression of nociceptive neurons in spinal cord directly, substance –P release is prevented ,prevents the neurotransmission in Aδ and C fibres and due to its interaction with α2 receptors in spinal and supraspinal sites.

So ,we in this study compared the effects of two different doses of clonidine and the following parameters were studied.

DEMOGRAPHIC VARIABLES :

AGE

The mean age in group -1 (clonidine 1mics/kg with bupivacaine 0.25% 1ml/kg) and group -2 (clonidine 2 mics/kg with bupivacaine 0.25%1ml/kg) are 3.42±1.12 and 3.52± 1.08 respectively with a p value of 0.8986 which is statistically not significant.

SEX

The sex in group -1 (clonidine 1mics/kg with bupivacaine 0.25%) and group -2 (clonidine 2 mics/kg with bupivacaine 0.25%) are comparable with a p value of 0.5 which is statistically not significant.

WEIGHT :

The mean weight in group -1 (clonidine 1mics/kg with bupivacaine 0.25%) and group -2 (clonidine 2 mics/kg with bupivacaine 0.25%) are11.8±3.4 and 11.2±2.6 respectively with a p value of 0.8163 which is statistically not significant.

TYPE OF SURGERY

The type of surgery in group -1 (clonidine 1mics/kg with bupivacaine 0.25% 1ml/kg) and group -2 (clonidine 2 mics/kg with bupivacaine 0.25% 1ml/kg) are comparable .

DURATION OF SURGERY

The mean duration of surgery in group -1 (clonidine 1mics/kg with bupivacaine 0.25%) and group -2 (clonidine 2 mics/kg with bupivacaine 0.25%) are 47.2 ±9.4mins and 46.8± 8.5mins respectively with a p value of 0.8752 which is statistically not significant.

HEMODYNAMIC VARIABLES

There was no change in pulse rate , mean arterial pressure and SPO2 during preoperative ,intraoperative and postoperative period . The two groups were comparable and the values wasfound statistically insignificant. The findings of this study correlated with similar studies done by Jamali et al and Cook et al.

MEAN DURATION OF POSTOPERATIVE ANALGESIA

The mean duration of postoperative analgesia in group 1 (clonidine 1mics/kg with bupivacaine 0.25% 1ml/kg) and group 2 (clonidine 2 mics/kg with bupivacaine 0.25% 1ml/kg) are 7±0.71hrsand 9.02± 0.5hrs respectively with a p value of <0.001 which was statistically significant .

The findings of this study well correlated with similar other studies done by T.S.Yildiz et al ,Archanakoul et al andLee and etal .

VOLUME OF LOCAL ANAESTHETICS

In this study bupivacaine 0.25% was used in the volume of 1ml/kg.

Sharpe et al reported that thevolume and concentration of bupivacaine must be adequate to bring about the action of clonidine , volume of 0.5ml /kg of bupivacaine will cause clonidine to settle caudally.

Similarly ,Hansen et al also conducted a study in children with three different concentrations of bupivacaine with clonidine 1mics/kg . They reported that the action of clonidine depends on the concentration and volume of bupivacaine administrated caudally.They concluded that there is no benefit of adding clonidine to 0.125% bupivacaine.

FLACC SCALE

FLACC scale was used in this study to assess pain.It was selected as it is easy to perform.The meannumber of doses of RESCUE ANALGESIA between group 1 (clonidine 1mics/kg with bupivacaine 0.25%) and group -2 (clonidine 2 mics/kg with bupivacaine 0.25%) are 1.52±1.05 and 0.92±0.91 respectively with a p value of 0.00354 and was found to be statistically significant.

So the above findings correlates well with similar studies donebyKlimscha et al al ,Motsch et al and Negri et al.

FLACC SCALE was not statistically significant at 2 hrs , 6hrs ,8 hrs and was found to be statistically significant at 10 hrswith a p value of 0.009.

COMPLICATIONS

There was no single occurrence of side effects like respiratory depression, bradycardia and hypotension between the two groups . Incidence of nausea and vomiting between the two groups were statistically insignificant with a p value of 0.5.

So these findings correlate with the studies performed by Anand MDhev et al and Tripi et al .

SUMMARY

This prospective randomized study was conducted in 50 children of age 2-6yrs posted for infraumbilical surgery .This study was done to compare the effects of two different doses of clonidine using ultrasound guided caudal block for postoperative analgesia in children. They were divided into two groups ,

group 1 receiving bupivacaine 0.25% (1ml/kg) with clonidine 1 mics /kg .

group 2 receiving bupivacaine 0.25% (1ml/kg) with clonidine 2 mics/kg.

Intraoperatively , monitors like MAP,pulse rate and spo2 were observed.In the post operative period, hemodynamic parameters like pulse rate, spo2 and MAP were noted ,pain was assessed by FLACC scale , the mean duration of postoperative analgesia and the number of doses of rescue analgesia and complications like respiratory depression,hypotension,bradycardia , vomiting were also noted.

According to the study , duration of post operative analgesia was prolonged with clonidine 2 mics/kg than clonidine 1 mics/kg group with a mean of 9 hrsvs 7.1hrs , the number of doses of rescue analgesia was reduced in clonidine 2 mics/kg group as well as FLACC scale score remain statistically significant at 10 hrs between two groups .

The hemodynamic parameters were well maintained in both groups , there was no incidence of respiratory depression, hypotension and bradycardia.

Hence Clonidine 2 mics/kg can be safely used in paediatrics as it has prolonged duration of post operativeanalgesia as well as it is devoid of side effects.

CONCLUSION

In conclusion, the data and statistical analysis suggest that in caudal block clonidine 2 mics/kg has prolonged duration of postoperative analgesia than clonidine 1 mics/kg and it also has minimal side effects. Hence Clonidine 2mics/kg can be used safely in caudal block for post operative analgesia in children.

BIBLIOGRAPHY

1. De Beer DA, Thomas ML. Caudal additives in children solutions or problems? Br J Anaesth 2003;90:487-98.
2. Ansermino M, Basu R, Vandebeek C, Montgomery C. Nonopioid additives to local anaesthetics for caudal blockade in children: A systematic review. PaediatrAnaesth 2003;13:561-73.
3. Kumar P, Rudra A, Pan AK, Acharya A. Caudal additives in pediatrics: A comparison among midazolam, ketamine, and neostigmine co-administered with bupivacaine. AnesthAnalg 2005;101:69-73.
4. Lonnqvist PA. Adjuncts to caudal block in children: Quo vadis? Br J Anaesth 2005;95:431-3.
5. Tsui BC, Berde CB. Caudal analgesia and anesthesia techniques in children. CurrOpinAnaesthesiol 2005;18:283-8.
6. Jamali S, Monin S, Begon C, Dubousset AM, Ecoffey C. Clonidine in pediatric caudal anesthesia. AnesthAnalg 1994;78:663-6.
7. Lee JJ, Rubin AP. Comparison of a bupivacaine-clonidine mixture with plain bupivacaine for caudal analgesia in children.Br J Anaesth 1994;72:258-62.
8. Tripi PA, Palmer JS. Clonidine increases duration of bupivacaine caudal analgesia for ureteroneocystostomy: A double blind prospective trial. J Urol 2005;174:1081-3.
9. Yildiz TS, Korkmaz F, Solak M, Toker K. Clonidine addition prolongs the

duration of caudal analgesia. ActaAnaesthesiolScand 2006;50:

10.Menzies R, Congreve K, Herodes V, Berg S, Mason D. A survey of pediatric caudal extradural anesthesia practice. PaediatrAnaesth 2009;19:829-36.

11.Cook B, Grubb DJ, Aldridge LA, Doyle E. Comparison of the effects of adrenaline, clonidine and ketamine on the duration of caudal analgesia produced by bupivacaine in children. Br J Anaesth 1995;75:698-701.

12.Luz G, Innerhofer P, Oswald E, Salner E, Hager J, Sparr H. Comparison of clonidine 1mcg/kg with morphine 30 mcg/kg for post-operative caudal analgesia in children. Eur J Anaesthesiol 1999;16:42-6.

13.Motsch J, Bottiger BW, Bach A, Bohrer H, Skoberne T, Martin E. Caudal clonidine and bupivacaine for combined epidural and general anaesthesia in children. ActaAnaesthesiolScand 1997;41:877-83.

14.Vetter TR, Carvallo D, Johnson JL, Mazurek MS, Presson RG Jr. A comparison of single-dose caudal clonidine, morphine, or hydromorphone combined with ropivacaine in pediatric patients undergoing ureteral reimplantation. AnesthAnalg 2007;104:1356-63.

15.Merkel SI, Voepel-Lewis T, Shayevitz JR, Malviya S. The FLACC: A behavioral scale for scoring postoperative pain in young children. PediatrNurs 1997;23:293-7.

16.Koul A, Pant D, Sood J. Caudal clonidine in day-care paediatric surgery. Indian J Anaesth 2009;53:450-4.

17.Klimscha W, Chiari A, Michalek-Sauberer A, Wildling E, Lerche A, Lorber C. The efficacy and safety of a clonidine/bupivacaine combination in caudal blockade for pediatric hernia repair. AnesthAnalg 1998;86:54-61.

18.Hager H, Marhofer P, Sitzwohl C, Adler L, Kettner S, Semsroth M. Caudal clonidine prolongs analgesia of caudal ketamine in children.AnesthAnalg 2002;94:1169-72.

19.Nishina K, Mikawa K. Clonidine in paediatricanaesthesia. CurrOpinAnaesthesiol 2002;15:309-16.

20.Breschan C, Krumpholz R, Likar R, Kraschl R, Schalk HV. Can a dose of 2 mcg/kg caudal clonidine cause respiratory depression in neonates? PaediatrAnaesth 1999;9:81-3.

21.Joshi W, Connelly NR, Freeman K, Reuben SS. Analgesic effect of clonidine added to bupivacaine 0.125% in paediatric caudal blockade. PaediatrAnaesth 2004;14:483-6.

22.Wheeler M, Patel A, Suresh S, Roth AG, Birmingham PK, Heffner CL. The addition of clonidine 2 mcg/kg does not enhance the postoperative analgesia of a caudal block using 0.125% bupivacaine and epinephrine 1:200,000 in children: A prospective, double-blind, randomized study. PaediatrAnaesth 2005;15:476-83.

23.Sharpe P, Klein JR, Thompson JP, Rushman SC, Sherwin J, Wandless JG. Analgesia for circumcision in a paediatric population: Comparison of caudal

bupivacaine alone with bupivacaine plus two doses of clonidine. PaediatrAnaesth 2001;11:695-700.

24. De Mey JC, Strobbet J, Poelaert J, Hoebeke P, Mortier. The influence of sufentanil and/or clonidine on the duration of analgesia after a caudal block for hypospadias repair surgery in children. Eur J Anaesthesiol 2000;17.

PROFORMA

NAME : **I.P.NO:** **ASA :**

AGE & SEX:

WEIGHT :

DATE&TIME OF ADMISSION: **DATE& TIME OF DISCHARGE:**

DIAGNOSIS:

PROCEDURE:

HISTORY: ALLERGY TO DRUGS, BLEEDING DISORDERS, CARDIAC AND RESPIRATORY DISEASES..

CLINICAL EXAMINATION: PR,BP, SPO2, RS, CVS.

BASIC INVESTIGATIONS:

HAEMOGLOBIN

RENAL PARAMETERS &SERUM ELECTROLYTES,

CHEST X RAY PA VIEW

ANAESTHETIC TECHNIQUE: USG GUIDED CAUDAL WITH TWO DIFFERENT DOSES OF CLONIDINE.

DOSAGE OF DRUG:

GROUP A : 1mL/kg of 0.25% bupivacaine with 1 mics/kg of clonidine.

GROUP B : 1ml/kg of 0.25% bupivacaine with 2 mics /kg of clonidine.

INTRA OPERATIVE

MONITORING OF VITALS .

monitors	5 min	10 min	15 min	20min	30min	40min	60min
Pulse rate							
MAP							
Spo2							

POST OPERATIVE PERIOD

ASSESSMENT OF PAIN FOR 10hrs

TECHNIQUE RELATED PAIN: FLACC SCORE BETWEEN 0 TO 10.

0 MEANING NO PAIN

10 MEANING EXCRUCIATING PAIN

PAIN WAS ASSESSED AT 0, 2 ,6 ,8 , 10 HRS POST OPERATIVELY.

MONITORING OF VITALS

Monitors	15min	20min	60min	90min	2hr	4hr	6hr	8hr	10hr
PULSE RATE									
MAP									
SPO2									

QUESTIONAIRRES USED IN THE STUDY

1) H/O any Known allergy to Local Anaesthetics/ any drugs

2) H/O any Neurological deficit

3) H/O any Bleeding diathesis

4) Any infection/Local sepsis at BLOCK site.

5) h/o any sacral bone deformities.

MASTER CHART Group 1 (Clonidine-1mics/kg with 0.25% bupivacaine 1ml/ kg)

S.NO	Name	Age	Sex	Wt. (KG)	Duration of surgery (MINS)	Type of surgery	Pulse rate																MAP															
							preop	Intraop							Postop								preop	Intraop							Postop								
								5min	10min	15min	20min	30min	40min	60min	15min	30min	60min	90min	2hr	4hr	6hr	8hr	10hr		5min	10min	15min	20min	30min	40min	60min	15min	30min	60min	90min	2hr	4hr	6hr	8hr	10hr
1	muthu	3	m	14	30	hernio rt	90	90	90	88	93	92	92	91	93	90	92	91	90	92	90	92	93	84	74	75	76	75	74	72	74	74	75	76	75	74	72	74	75	74
2	raja	2	m	10	40	hernio rt	88	97	89	98	92	92	90	90	93	94	93	92	92	91	92	93	92	83	73	74	72	73	72	72	74	73	74	72	73	72	72	74	75	76
3	siva	5	m	10	45	hernio rt	89	98	87	86	93	91	91	92	93	91	92	92	91	90	91	92	93	77	75	74	72	72	72	74	75	75	74	72	72	72	74	75	75	75
4	arun	3	m	14	60	hernio lt	91	96	86	95	94	90	89	88	92	93	92	92	93	93	92	93	93	78	73	76	72	73	74	74	75	73	76	72	73	74	74	75	76	75
5	madhan	4	m	13	50	hernio rt	90	95	94	94	92	93	88	88	93	93	91	90	92	91	92	90	92	74	74	76	76	73	73	76	74	74	76	76	73	73	76	74	74	76
6	gopal	2	m	19	45	hernio rt	98	94	95	90	95	93	90	90	92	92	93	93	92	92	92	93	92	76	73	76	74	72	72	77	75	73	76	74	72	72	77	75	75	76
7	vijay	5	m	10	60	hernio lt	99	94	94	92	95	93	91	91	91	93	91	92	93	90	95	94	98	73	72	75	73	72	71	78	74	72	75	73	72	71	78	74	74	75
8	karthi	6	m	8	40	hernio rt	87	93	92	92	96	92	92	92	92	93	96	93	94	90	89	92	89	72	74	74	73	71	71	76	75	74	74	73	71	71	76	75	76	76
9	jeeva	4	m	10	30	hernio lt	98	93	93	93	94	91	93	93	95	92	93	94	92	90	92	93	94	70	73	73	74	73	72	77	74	73	73	74	73	72	77	74	75	76
10	selvan	2	m	12	35	hernio rt	99	92	93	92	90	90	94	94	93	91	94	93	95	89	92	92	91	73	72	73	72	74	71	75	75	72	73	72	74	71	75	75	75	74
11	moorthy	2	m	12	55	hernio rt	90	93	91	90	90	89	93	93	92	92	92	94	94	94	93	95	94	72	75	74	74	71	72	75	73	75	74	74	71	72	75	73	73	75
12	murali	4	m	10	45	orchido	89	93	95	92	90	92	87	94	94	92	93	92	91	92	93	93	95	72	74	77	73	75	74	76	75	74	77	73	75	74	76	75	74	74
13	bala	2	m	15	35	hernio rt	98	89	88	90	90	93	88	95	93	91	94	90	91	92	93	98	92	75	73	75	72	72	74	75	74	73	75	72	72	74	75	74	73	73
14	ravi	4	m	20	60	hernio lt	88	95	80	94	93	94	98	98	91	92	93	91	90	92	93	94	95	75	72	74	73	73	74	75	73	72	74	73	73	74	75	73	74	73
15	senthil	3	m	5	45	orchido	99	92	85	95	92	95	97	98	93	92	94	93	92	90	92	92	93	73	73	73	73	74	74	74	74	73	73	73	74	74	74	74	74	73
16	saravanan	3	m	10	55	hernio lt	90	93	90	93	92	98	92	97	92	91	94	90	93	90	92	90	92	72	75	72	74	76	75	74	73	75	72	74	76	75	74	73	74	74
17	ganesh	4	m	14	45	hernio rt	88	94	89	90	90	92	94	94	93	92	93	91	94	94	93	92	91	78	74	74	72	73	74	75	75	74	74	72	73	74	75	75	75	72
18	chitra	4	f	15	60	hernio rt.	90	95	88	94	90	95	90	93	92	90	92	92	93	95	93	89	94	78	75	75	73	74	74	76	76	75	75	73	74	74	76	76	76	73
19	rani	2	f	12	45	hernio rt.	94	90	91	95	95	92	92	92	92	94	92	93	92	92	90	92	92	79	74	74	73	74	74	75	74	74	74	73	74	74	75	74	74	73
20	selvi	3	f	12	50	hernio lt	90	90	92	96	93	94	91	91	93	92	93	92	93	92	90	89	95	73	78	74	73	73	74	75	74	78	74	73	73	74	75	74	73	74
21	angel	3	f	10	40	hernio rt.	99	95	91	92	92	93	93	94	90	91	94	95	94	93	91	90	94	74	77	76	75	74	73	74	73	77	76	75	74	73	74	73	72	73
22	chandran	4	m	12	45	orchido	90	92	90	92	88	92	93	92	91	91	94	93	96	92	89	90	93	73	74	76	75	74	74	72	72	74	76	75	74	74	72	72	73	75
23	muthu	5	m	10	50	hernio lt.	99	90	93	92	96	89	89	93	92	93	93	92	92	93	98	91	92	72	75	75	75	75	75	73	72	75	75	75	75	75	73	72	74	74
24	veni	4	f	6	60	hernio rt.	88	92	89	94	95	90	90	90	94	92	93	92	91	92	91	94	93	70	74	75	74	74	73	73	73	74	75	74	74	73	73	73	74	73
25	velu	4	m	12	55	orchido	89	92	90	93	94	91	91	91	92	91	90	92	90	90	91	92	93	77	75	76	74	75	73	73	73	75	76	74	75	73	73	73	75	74

SPO2																		Duration of postopanalgesia (Hrs.)	No of dose of rescue analgesia	Flacc Pain Scale				COMPLICATIONS				
	Intraop							Postop												2HR	6HR	8HR	10HR					
preop	5min	10min	15min	20min	30min	40min	60min	15min	30min	60min	90min	2hr	4hr	6hr	8hr	10hr				Pain	Pain	Pain	Pain	NAUSEA	VOMITING	HYPOTENSION	RESPIRATORY DEPRESSION	BRADYCARDIA
98	98	98	98	98	99	98	98	99	98	99	98	99	98	99	98	98	6	1	mild/no	mild/no	mod/sev	mod/sev	nil	nil	nil	nil	nil
99	98	99	98	99	98	99	98	98	98	98	98	98	99	98	98	99	7	0	mild/no	mild/no	mod/sev	mod/sev	nil	nil	nil	nil	nil
98	98	99	98	99	98	99	98	99	98	99	98	99	98	99	98	98	5.5	2	mild/no	mod/sev	mod/sev	mod/sev	present	nil	nil	nil	nil
99	98	99	98	99	98	99	98	98	98	99	98	99	98	99	98	99	7.5	0	mild/no	mild/no	mild/no	mod/sev	nil	nil	nil	nil	nil
98	98	99	98	99	98	99	98	98	98	99	98	99	98	99	98	98	8	1	mild/no	mild/no	mild/no	mod/sev	nil	nil	nil	nil	nil
99	97	98	98	98	99	98	99	99	98	99	98	99	98	99	98	98	7.5	1	mild/no	mod/sev	mod/sev	mod/sev	nil	nil	nil	nil	nil
98	98	98	98	99	99	97	97	98	97	98	97	98	99	98	99	98	6.5	3	mild/no	mild/no	mod/sev	mod/sev	nil	nil	nil	nil	nil
99	99	98	98	99	99	97	97	98	98	98	98	99	99	97	97	98	6.5	2	mild/no	mild/no	mod/sev	mild/no	nil	nil	nil	nil	nil
99	98	98	98	98	99	98	98	99	99	98	98	99	99	97	97	99	7.5	1	mild/no	mild/no	mild/no	mod/sev	nil	nil	nil	nil	nil
98	99	99	97	98	99	99	99	98	98	98	98	98	99	98	98	98	7	1	mild/no	mild/no	mod/sev	mod/sev	nil	nil	nil	nil	nil
99	98	98	99	98	98	98	98	99	99	99	97	98	99	99	99	98	8	1	mild/no	mild/no	mild/no	mild/no	present	nil	nil	nil	nil
100	98	99	98	98	99	99	98	99	98	98	97	98	98	98	98	98	7.5	1	mild/no	mild/no	mild/no	mod/sev	nil	present	nil	nil	nil
98	98	98	98	98	98	98	99	98	98	99	98	98	99	99	98	99	8	0	mod/sev	mild/no	mod/sev	mild/no	nil	nil	nil	nil	nil
97	98	99	99	99	99	98	99	99	98	98	98	98	98	98	99	98	6	3	mild/no	mild/no	mod/sev	mod/sev	nil	nil	nil	nil	nil
99	98	98	98	98	99	97	99	99	98	99	97	99	99	98	99	98	6.5	3	mild/no	mild/no	mod/sev	mod/sev	nil	nil	nil	nil	nil
98	98	99	98	99	98	98	98	98	98	98	98	98	99	97	99	99	7	2	mild/no	mild/no	mod/sev	mod/sev	nil	present	nil	nil	nil
99	99	99	99	98	99	99	98	98	98	99	98	99	98	98	98	99	6	3	mod/sev	mod/sev	mod/sev	mod/sev	nil	nil	nil	nil	nil
98	98	98	99	98	98	98	99	99	99	99	99	98	99	99	98	98	6.5	2	mild/no	mod/sev	mild/no	mod/sev	nil	nil	nil	nil	nil
99	99	98	98	97	99	99	98	97	98	98	99	98	98	98	99	99	7	1	mild/no	mild/no	mod/sev	mod/sev	nil	nil	nil	nil	nil
99	97	98	99	98	99	98	99	98	99	98	98	97	99	99	98	99	7.5	1	mild/no	mild/no	mod/sev	mod/sev	nil	nil	nil	nil	nil
98	98	98	99	98	99	99	98	99	97	98	99	98	99	98	99	98	8	0	mild/no	mild/no	mod/sev	mod/sev	nil	present	nil	nil	nil
97	99	99	98	98	99	98	98	98	98	98	99	98	99	99	98	99	7	1	mod/sev	mod/sev	mod/sev	mod/sev	nil	nil	nil	nil	nil
99	98	98	98	98	99	99	98	98	99	99	98	98	99	98	98	98	7.5	1	mild/no	mild/no	mod/sev	mod/sev	nil	nil	nil	nil	nil
99	99	98	98	98	99	98	99	99	98	98	98	98	99	99	98	99	7	2	mod/sev	mod/sev	mod/sev	mod/sev	nil	nil	nil	nil	nil
98	98	99	98	98	99	99	98	98	99	98	98	98	99	98	99	98	6.5	3	mild/no	mod/sev	mod/sev	mod/sev	nil	nil	nil	nil	nil

MASTER CHART Group 2 (Clonidine-2mics/kg with 0.25% bupivacaine 1ml/ kg)

S.NO	Name	Age	Sex	Wt. (KG)	Duration of surgery (MINS)	Type of surgery	Pulse rate																MAP															
							preop	Intraop							Postop								preop	Intraop							Postop								
								5min	10min	15min	20min	30min	40min	60min	15min	30min	60min	90min	2hr	4hr	6hr	8hr	10hr		5min	10min	15min	20min	30min	40min	60min	15min	30min	60min	90min	2hr	4hr	6hr	8hr	10hr
1	sundar	2	m	14	40	hernio rt	98	93	95	88	93	92	92	91	93	93	90	92	91	90	92	90	92	84	74	75	76	75	74	72	74	74	75	76	75	74	73	74	75	74
2	sankar	4	m	10	40	hernio rt	90	97	94	98	90	92	91	92	92	93	94	93	92	92	91	92	93	77	73	74	72	76	72	72	74	73	74	75	73	73	74	74	75	76
3	ajay	2	m	10	45	hernio rt	94	98	88	92	89	94	91	92	93	93	91	92	92	91	90	91	92	76	75	74	72	75	72	74	75	75	74	72	72	74	74	75	75	75
4	arjun	5	m	10	60	hernio lt	93	96	89	95	89	90	91	93	92	92	93	92	92	93	93	92	93	78	73	76	72	76	74	74	75	73	76	74	73	74	74	75	76	75
5	sunil	4	m	14	50	hernio rt	90	95	90	94	90	91	90	92	92	93	93	91	90	92	91	92	90	80	74	76	76	73	73	76	74	74	76	76	73	73	76	74	74	76
6	surya	2	m	12	40	hernio rt	99	94	90	90	89	90	91	92	98	92	92	93	93	92	92	92	93	74	73	76	74	75	72	77	78	74	76	74	72	74	77	75	75	76
7	bharathy	3	f	7	45	hernio rt	93	94	89	92	88	92	92	92	89	91	93	91	92	93	90	95	94	75	72	75	74	72	71	78	74	74	75	73	72	73	78	74	74	75
8	boopathy	5	m	15	60	hernio lt	94	93	89	92	91	94	93	92	94	92	93	96	93	94	90	89	92	74	74	74	73	76	76	76	75	74	74	73	71	73	76	75	76	76
9	giri	4	m	12	40	hernio lt	90	93	92	93	89	93	92	93	91	95	92	93	94	92	90	92	93	73	73	73	74	73	72	77	74	73	73	74	73	72	77	74	75	76
10	kannan	2	m	10	30	hernio rt	93	92	93	92	89	92	93	92	91	93	91	94	93	95	89	92	92	74	72	73	72	74	76	75	75	72	73	72	74	74	75	75	75	74
11	gowri	3	f	12	45	hernio rt	94	93	92	90	89	93	92	95	94	92	92	92	94	94	94	93	95	72	75	74	74	71	72	75	73	75	74	74	71	72	75	75	73	75
12	panju	4	m	15	55	orchido	90	89	93	92	94	89	94	94	95	94	92	93	92	91	92	93	93	72	74	77	73	75	74	76	75	74	77	73	75	74	76	75	74	74
13	palani	3	m	10	35	hernio rt	92	95	93	94	94	93	92	93	93	93	91	94	90	91	92	93	98	75	73	75	72	72	74	75	74	73	75	72	72	74	75	74	73	73
14	guna	6	m	18	35	hernio lt	93	92	92	94	94	93	93	92	92	91	92	93	91	90	92	93	94	75	72	74	73	73	74	75	73	72	74	73	73	74	75	73	74	73
15	krishna	4	m	8	45	orchido	90	93	93	95	93	93	92	94	91	93	92	94	93	92	90	92	92	73	73	73	73	74	74	74	74	73	73	73	74	74	74	74	74	73
16	bargavi	4	f	10	45	hernio rt	93	95	92	93	93	94	92	91	94	92	91	94	90	93	90	92	90	75	75	72	74	76	74	74	73	75	72	74	76	75	74	73	74	74
17	priya	3	f	15	55	hernio rt	94	94	91	94	93	92	95	93	93	93	92	93	91	94	94	93	92	77	74	74	72	73	74	75	75	74	74	76	73	74	75	75	75	72
18	preethi	3	m	14	45	hernio lt	95	90	88	92	92	93	94	93	92	92	90	92	92	93	95	93	89	76	75	75	73	74	74	76	76	75	75	75	74	74	76	76	76	73
19	adthiya	2	m	12	60	hernio lt	92	90	91	92	92	91	92	92	93	92	94	92	93	92	92	90	92	77	74	74	73	74	74	75	74	74	74	74	74	74	75	74	74	73
20	jegadeh	3	m	12	50	orchido	91	93	92	91	92	94	93	92	94	93	92	93	92	93	92	90	89	72	78	74	73	73	74	75	74	78	74	73	73	74	75	74	73	74
21	chandra	4	f	10	40	hernio rt	99	94	91	89	90	89	90	92	93	90	91	94	95	94	93	91	90	74	77	76	75	74	73	74	73	77	76	75	74	73	74	73	72	73
22	prem	3	m	10	50	orchido	98	92	90	92	92	90	95	90	93	91	91	94	93	96	92	89	90	73	74	76	75	74	74	72	72	74	76	75	74	74	72	72	73	75
23	malar	4	f	12	45	hernio rt	90	90	93	92	91	93	92	92	94	92	93	93	92	92	93	98	91	75	75	75	75	75	75	73	72	75	75	75	75	75	73	72	74	74
24	sahul	5	m	10	55	hernio lt	88	92	89	94	95	90	90	91	94	94	92	93	92	91	92	91	94	70	74	75	74	74	73	73	73	74	75	74	74	73	73	73	74	73
25	shakthi	4	m	8	60	orchido	90	92	90	94	92	92	93	92	93	92	91	90	92	90	90	91	92	75	75	76	74	75	73	73	73	75	76	74	75	73	73	73	75	74

SPO2																	Duration of postopanalgesia (Hrs.)	No of dose of rescue analgesia	Flacc Pain Scale				COMPLICATIONS				
preop	Intraop							Postop											2HR	6HR	8HR	10HR					
	5min	10min	15min	20min	30min	40min	60min	15min	30min	60min	90min	2hr	4hr	6hr	8hr	10hr			Pain	Pain	Pain	Pain	NAUSEA	VOMITING	HYPOTENSION	RESPIRATORY DEPRESSION	BRADYCARDIA
98	98	99	98	99	98	99	98	99	98	99	98	99	98	99	98	98	8.5	1	mild/no	mild/no	mild/no	mod/sev	nil	nil	nil	nil	nil
99	98	98	98	98	99	98	98	98	98	98	98	98	99	98	98	99	8.5	2	mild/no	mild/no	mild/no	mod/sev	nil	nil	nil	nil	nil
99	98	99	98	99	98	99	98	99	98	99	98	99	98	99	98	98	9.5	0	mild/no	mild/no	mild/no	mild/no	nil	nil	nil	nil	nil
98	98	99	98	99	98	99	98	98	98	99	98	99	98	99	98	99	9.5	0	mild/no	mild/no	mild/no	mild/no	nil	nil	nil	nil	nil
99	98	99	98	99	98	99	98	98	98	99	98	99	98	99	98	98	8.5	2	mild/no	mild/no	mod/sev	mod/sev	nil	nil	nil	nil	nil
99	98	99	98	99	98	99	98	99	98	99	98	99	98	99	98	98	8	2	mild/no	mild/no	mild/no	mild/no	nil	nil	nil	nil	nil
98	97	98	99	98	99	98	99	98	97	98	97	98	99	98	99	98	9.5	0	mild/no	mild/no	mild/no	mild/no	nil	nil	nil	nil	nil
100	98	98	98	99	99	97	97	98	98	98	98	99	97	97	97	98	10	0	mild/no	mild/no	mild/no	mild/no	nil	nil	nil	nil	nil
100	99	98	98	99	99	97	97	99	99	98	98	99	99	97	97	99	9	1	mild/no	mild/no	mod/sev	mod/sev	nil	nil	nil	nil	nil
99	98	98	98	98	99	98	98	98	98	98	98	98	99	98	98	98	9	1	mild/no	mild/no	mild/no	mild/no	nil	nil	nil	nil	nil
98	99	99	98	98	99	99	99	99	99	97	97	98	99	99	99	97	9.5	0	mild/no	mild/no	mild/no	mild/no	present	nil	nil	nil	nil
99	98	98	97	98	98	98	98	99	98	98	97	98	98	98	98	97	9	1	mild/no	mild/no	mild/no	mild/no	nil	nil	nil	nil	nil
99	98	99	98	98	99	99	98	98	98	99	98	98	99	99	98	99	9	0	mild/no	mod/sev	mod/sev	mod/sev	nil	nil	nil	nil	nil
98	98	98	98	98	98	98	99	99	98	98	98	98	98	98	99	98	8.5	2	mild/no	mild/no	mod/sev	mod/sev	nil	nil	nil	nil	nil
99	98	99	97	99	99	98	99	99	98	99	97	99	99	98	99	98	9.5	0	mild/no	mild/no	mod/sev	mod/sev	nil	nil	nil	nil	nil
99	98	98	98	98	99	97	99	98	98	98	98	98	99	97	99	99	9	1	mild/no	mild/no	mod/sev	mod/sev	nil	present	nil	nil	nil
98	98	99	98	99	98	98	98	98	98	99	98	99	98	98	98	99	9.5	0	mod/sev	mod/sev	mod/sev	mod/sev	nil	nil	nil	nil	nil
99	99	99	99	98	99	99	98	99	99	99	99	98	99	99	98	98	9	1	mild/no	mild/no	mod/sev	mod/sev	nil	nil	nil	nil	nil
98	98	98	99	98	98	98	99	97	98	98	99	98	98	98	99	99	8	3	mild/no	mild/no	mod/sev	mod/sev	nil	nil	nil	nil	nil
99	99	98	98	97	99	99	98	98	99	98	98	97	99	99	98	99	9	1	mild/no	mild/no	mild/no	mild/no	nil	nil	nil	nil	nil
98	97	98	99	98	99	98	99	99	97	98	99	98	99	98	99	98	10	0	mild/no	mild/no	mild/no	mild/no	nil	present	nil	nil	nil
99	98	98	99	98	99	99	98	98	98	98	99	98	99	99	98	99	9.5	1	mod/sev	mod/sev	mod/sev	mod/sev	nil	nil	nil	nil	nil
98	99	99	98	98	99	98	98	98	99	99	98	98	99	98	98	98	8.5	2	mild/no	mild/no	mod/sev	mod/sev	nil	nil	nil	nil	nil
99	98	98	98	98	99	99	98	99	98	98	98	98	99	99	98	99	9	0	mild/no	mod/sev	mod/sev	mod/sev	nil	nil	nil	nil	nil
99	99	98	98	98	99	98	99	98	99	98	98	98	99	98	99	98	8.5	2	mild/no	mod/sev	mod/sev	mod/sev	nil	nil	nil	nil	nil

COMPARISON OF TWO DIFFERENT DOSES OF CLONIDINE WITH ULTRASOUND GUIDED CAUDAL FOR POST OPERATIVE PAIN RELIEF IN CHILDREN.

DISSERTATION SUBMITTED FOR THE DEGREE OF

DOCTOR OF MEDICINE

BRANCH – X (ANAESTHESIOLOGY)

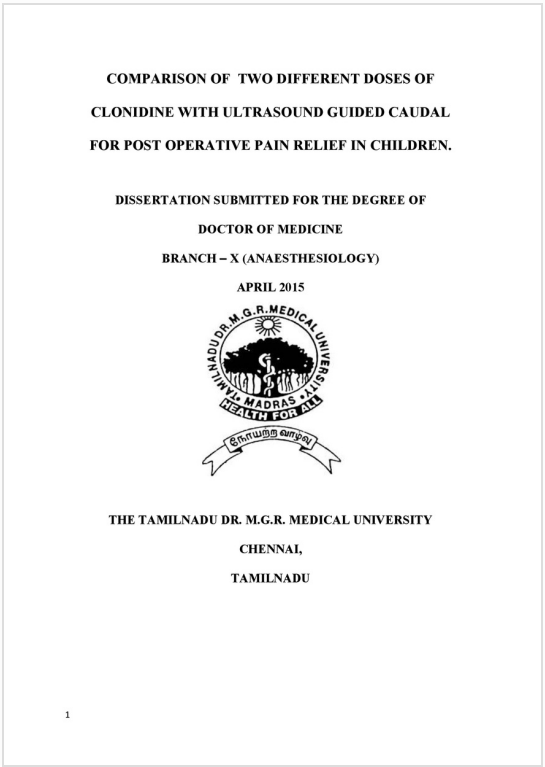
APRIL 2015

Digital Receipt

This receipt acknowledges that Turnitin received your paper. Below you will find the receipt information regarding your submission.

The first page of your submissions is displayed below.

Submission author:	201220101.md Anaesthesiology AMB.
Assignment title:	TNMGRMU EXAMINATIONS
Submission title:	COMPARISON OF TWO DIFFEREN..
File name:	ambikai_final_dissertation_21_9_14....
File size:	4.54M
Page count:	129
Word count:	15,162
Character count:	86,011
Submission date:	24-Sep-2014 08:38PM
Submission ID:	450255873



COMPARISON OF TWO DIFFERENT DOSES OF

CLONIDINE WITH ULTRASOUND GUIDED CAUDAL

FOR POST OPERATIVE PAIN RELIEF IN CHILDREN.

DISSERTATION SUBMITTED FOR THE DEGREE OF

DOCTOR OF MEDICINE

BRANCH – X (ANAESTHESIOLOGY)

APRIL 2015

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

CHENNAI,

TAMILNADU

1

Ref.No.4459/E1/5/2014

Madurai Medical College,
Maduai -20. Dated: 05 .2014.

Institutional Review Board/Independent Ethics Committee
Capt.Dr.B.Santhakumar,MD (FM). deanmdu@gmail.com
Dean, Madurai Medical College &
Government Rajaji Hospital, Madurai 625 020 . Convenor

Sub: Establishment – Madurai Medical College, Madurai-20 – Ethics Committee Meeting – Meeting Minutes - for May 2014 – Approved list – reg.

The Ethics Committee meeting of the Madurai Medical College, Madurai was held on 12th May 2014 at 10.00 Am to 12.00 Noon at Anaesthesia Seminar Hall at Govt. Rajaji Hospital, Madurai . The following members of the Ethics Committee have attended the meeting.

1.Dr.V.Nagarajan,M.D.,D.M(Neuro) Ph: 0452-2629629 Cell No.9843052029 nag9999@gmail.com.	Professor of Neurology (Retired) D.No.72, Vakkil New Street, Simmakkal, Madurai -1	Chairman
2.Dr.Mohan Prasad, MS.M.Ch. Cell.No.9843050822 (Oncology) drbkcmp@gmail.com	Professor & H.O.D of Surgical Oncology (Retired) D.No.32, West Avani Moola Street, Madurai.-1	Member Secretary
3.Dr.K.Parameswari, MD(Pharmacology) Cell No.9994026056 drparameswari@yahoo.com.	Director of Pharmacology Madurai Medical College.	Member
4.Dr.S.Vadivel Murugan, MD., (Gen.Medicine) Cell No.9566543048 svadivelmurugan_2007@rediffmail.com.	Professor & H.O.D of Medicine Madurai Medical College	Member
5. Dr.L.Santhanalakshmi, MD (Physiology) Cell No.9842593412 dr.l.santhanalakshmi@gmail.com.	Vice Principal, Prof. & H.O.D. Institute of Physiology Madurai Medical College	Member
6.Dr.A.Sankaramahalingam, MS., (Gen. Surgery) Cell.No.9443367312 chandrahospitalmdu@gmail.com	Professor & H.O.D. Surgery Madurai Medical College. Madurai	Member
7.Mrs.Mercy Immaculate Rubalatha, M.A., Med., Cell.No.9367792650 lathadevadoss86@gmail.com	50/5, Corporation Officer's Quarters, Gandhi Museum Road, Thamukam, Madurai-20.	Member
8.Thiru.Pala.Ramasamy, B.A.,B.L., Cell.No.9842165127 palaramasamy2011@gmail.com	Advocate, D.No.72,Palam Station Road, Sellur, Madurai-20.	Member
9.Thiru.P.K.M.Chelliah, B.A., Cell No.9894349599 pkmandco@gmail.com	Businessman, 21 Jawahar Street, Gandhi Nagar, Madurai-20.	Member

Name of P.G.	Course	Name of the Project	Remarks
Dr.D.Ambikai	PG in M.D. (Anaesthesiology), Madurai Medical College Madurai & Government Rajaji Hospital, Madurai.	Comparison of two different doses of clonidine with USG Guided caudal for post OP pain relief in children.	Approved

Please note that the investigator should adhere the following: She/He should get a detailed informed consent from the patients/participants and maintain it Confidentially.

1. She/He should carry out the work without detrimental to regular activities as well as without extra expenditure to the institution or to Government.
2. She/He should inform the institution Ethical Committee, in case of any change of study procedure, site and investigation or guide.
3. She/He should not deviate the area of the work for which applied for Ethical clearance. She/He should inform the IEC immediately, in case of any adverse events or Serious adverse reactions.
4. She/He should abide to the rules and regulations of the institution.
5. She/He should complete the work within the specific period and if any Extension of time is required He/She should apply for permission again and do the work.
6. She/He should submit the summary of the work to the Ethical Committee on Completion of the work.
7. She/He should not claim any funds from the institution while doing the work or on completion.
8. She/He should understand that the members of IEC have the right to monitor the work with prior intimation.

Member Secretary **Chairman**
Ethical Committee

DEAN/Convenor
Govt. Rajaji Hospital,
Madurai- 20.

04/12/13

To
The above Applicant
-thro. Head of the Department concerned

forwarded

DIRECTOR
INSTITUTE OF ANAESTHESIOLOGY
Madurai Medical College &
Govt. Rajaji Hospital
Madurai-625 020